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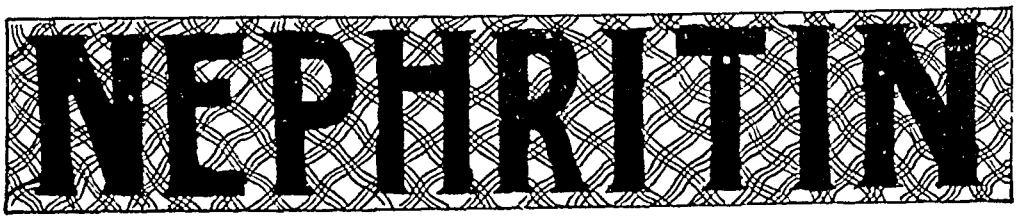

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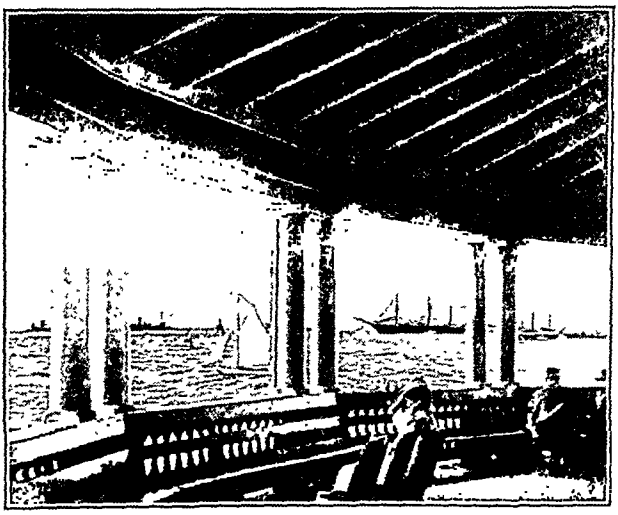

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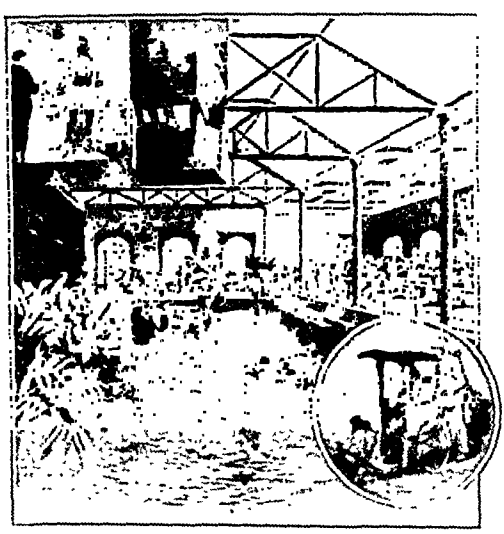

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

JUNE, 1907.

ORIGINAL ARTICLES.

TUBERCULIN IMMUNIZATION IN THE TREATMENT OF PULMONARY TUBERCULOSIS.

By E. L. Trudeau, M.D.,
of Saranac Lake, New York.

The specific treatment of tuberculosis by tuberculin is based on the principle of artificial immunization. The production of artificial immunity to tuberculosis has been long looked upon as impossible of attainment, because there is little clinical evidence that one attack protects from another. Nevertheless, the tireless and painstaking experimental work which has been carried on by many observers during the past fifteen years has done much to demonstrate the possibility of producing, artificially, in animals a certain degree of immunity. This immunity has been shown to be only relative, and the best results have been invariably attained thus far by vaccination with living bacilli, while the inoculations of culture products freed from germs or of bacteria killed by heat or other methods, though they have been found to be of some value, have never brought about as good results as vaccination with living germs. It is to the study of the mechanism of artificial immunization in animals that we must look to help us formulate a method of attempted immunization in the tuberculous patient; but unfortunately the mechanism of artificial immunization against tuberculosis, like that of all chronic infectious diseases, is as yet but very imperfectly understood, though our knowledge of the many defensive resources of the living organism against the toxin and the microbe itself is steadily growing. We know that there is an antitoxic immunity, an antibacterial immunity, and an immunity produced by

vaccination with living bacteria which follows as a result of the victory of the tissues over the living germ, and to which von Behring has given the name of isopathic immunity. The exact part played by the antitoxins, by the various antibodies, the agglutinins, the bacteriolysins, and the opsonins, is as yet imperfectly understood; but we may take if for granted that these are all part of the mechanism of immunization and factors in Nature's attempt to protect the body against bacterial infection. Wright's method of immunization accepts as the sole guide for dosage and intervals between doses one of these immunity reactions, as demonstrated by the opsonic index. One thing we may learn from the more recent studies on the production of artificial immunity to tuberculosis is that the dose of virus, whether living or dead, and the time which elapses between the protective inoculations and before exposure to reinfection, are essential elements on which success or failure may turn.

Calmette, in his recent studies of vaccination of calves and young goats through the intestinal tract by the introduction of living virulent tubercle bacilli, found that whether a localized process limited to the mesenteric glands and ultimately resulting in a marked degree of immunity or general infection resulted, depended entirely on the number of the bacilli introduced and the time which elapsed before another infection. A very small amount of infectious material becoming arrested in the intestinal and mesenteric glands, and attacked there by the leukocytes resulted in immunity to subsequent inoculations—inoculations which prove fatal to control animals—while a larger amount, or repeated inoculations of the same small dose, though arrested for a time in the mesenteric glands, passed on through the lymph stream into the circulation, and ended in general infection and the death of the animal.

Von Behring has found practically the same thing, and the work of Wright and Douglas on the opsonins shows that even when dead culture products are made use of, the size of the dose governs the result, which may be a prolonged negative phase with its decrease of the natural resisting power, or a positive phase resulting in a relative degree of immunization. If we use tuberculin by the clinical method we notice the same thing; namely, that infinitesimal doses, methodically increased, which produce only slight stimulation of the defensive resources of the organism, result in a well-marked degree of toxin immunity, as shown by increased toleration to large doses of toxin, while larger doses or too rapid an increase, may bring about hypersusceptibility and an aggravation of all the symptoms of the disease.

The importance of time in the production of artificial immunization has also been thoroughly demonstrated. It seems that whatever degree of immunity it is possible to produce is produced only very slowly. Von Behring found that his vaccinated cows

which received the virulent inoculation before three months had passed showed little immunity and generally died of the infection, while after three months they resisted a fatal dose of the virus. Experimental evidence, therefore, teaches that the dose of the vaccine and the time occupied by the treatment, as well as the time which elapses between doses, must prove cardinal points in any attempted method of inoculation with bacterial products, and clinical study of tuberculin treatment in man leads to the same conclusion. While the principle of artificial immunity seems to be fairly well established by animal experimentation, it must be admitted that the laboratory evidence which bears on the production of immunity in animals, or the cure of experimental tuberculosis by tuberculin, is far from satisfactory. Even Koch has failed to give the details of the experiments in which he claims to have protected guinea-pigs against infection by treatment with his two immunizing tuberculins, T. R. and B. E., and he contents himself with simply stating that this can be done. I know of no one else, however, who has cured experimental tuberculosis in the guinea-pig, and I have always failed to do so myself. Behring, like Koch, claims to protect guinea-pigs, but gives no facts.

The best results I have obtained in treating animals with tuberculin have been shown in the eye tuberculosis of the rabbit, which is naturally a chronic and almost always a purely localized process. Tuberculosis in the guinea-pig, on the other hand, is an acute progressive infection, and experimental and clinical evidence are in perfect accord in demonstrating that against the acute types of tuberculous infection tuberculin is powerless, whether it be employed in man or animals.

The duration of artificial immunity, such as has been successfully produced so far in animals, has not yet been ascertained, but the evidence so far at hand points to the fact that as the most solid immunity is produced by living though attenuated cultures, the immunity which lasts the longest is also brought about in this way, the antitoxic immunity produced by bacterial products being of much shorter duration. This is perhaps not as discouraging as it might at first sight appear, because in our therapeutic attempts at immunization with dead bacterial products the patient already has within his tissues the living organism, the victory over which seems so essential to the production of the most solid immunity, and if by properly spaced and properly graded inoculations of bacterial products we may assist him to overcome his infection, the immunity thus obtained might be quite durable.

TUBERCULINS. Koch, to whom we owe the discovery of tuberculin, was also the first to propose its therapeutic employment. Curiously enough, he did not at first consider his old tuberculin as an immunizing agent, but thought the local reactions it produced resulted in a necrotic process which ended in the discharge of the

dead and diseased tissue and healing of the lesion. His original tuberculin is made by evaporating by heat liquid cultures to a tenth of their original volume, and filtering off the bacilli through a porcelain filter. This tuberculin, which he called a glycerin extract of the tubercle bacillus, is the one which is used for the tuberculin test both in man and animals, as well as therapeutically. His two more recent tuberculins, T. R. and B. E., represent attempts at producing antitoxic and antibacterial immunity, and are suspensions of crushed tubercle bacilli in glycerin and water. Many other tuberculins have been proposed during the past fifteen years, among which I may mention Hunter's Modification B., von Ruck's Watery Extract, Landemann's Tuberculol, Denys' B. F., Baraneck's Tuberculins, Spengler's Bovine B. F., and Behring's T. C. and Tulasa, which he claims immunizes cows as well as the living bacilli, but the value of which has not yet been put to a practical test in the treatment of human tuberculosis. These tuberculins are all vaccines, they are all made from either the body substance of the germ or the liquid medium in which it has grown, or both, and their aim is to stimulate the defensive resources of the system and to induce antitoxic and antibacterial immunity. They all produce, when given in sufficient doses, local reactions in tuberculous foci, and the well-known but little understood phenomena of general tuberculin reaction.

Koch's old tuberculin principally has been used at the Adirondack Cottage Sanitarium, but of late I have discarded it, because I prefer an immunizing agent in the preparation of which no heat has been used, and I make use of either B. F., which is merely a filtrate of human cultures of recorded virulence grown in my own laboratory, to which a quarter of 1 per cent. carbolic acid has been added, or B. E., which is an emulsion in glycerin and water of the pulverized bodies of virulent tubercle bacilli. The first, which is known as Denys' tuberculin, and for which he has a strong preference, contains all the toxins and other substances which may be produced by the growth of the bacilli or dissolved from their disintegrating bodies in a liquid medium; and the second, which is Koch's last attempt at producing an immunizing substance, contains the toxins and endotoxins to be found in the bodies of the crushed germs entire and unaltered by heat or chemicals.

The use of B. F., from bovine cultures, was proposed by Spengler, and it is possible that in infections of bovine origin it may be preferable to tuberculin made from tubercle bacilli of human origin. I am applying it in a few cases in which the patient does not seem to be making any improvement while treated with B. F. of human origin.

Reasoning from analogy and what we know of artificial immunity in other bacterial infections, an antitoxic immunity would be more likely to be produced by the old tuberculin and the B. F., which

contain the toxins elaborated by the growth of the germs in a liquid medium, while the B. E., which holds in suspension the crushed body substance of the tubercle bacilli, might be expected to produce a greater degree of antibacterial immunity.

I am not a partisan of any particular tuberculin, but I use the B. F. at present more extensively than the B. E., only because I am more familiar with its use, and because it is easier to control in its effects. With the B. E. habituation takes place with much more difficulty, and occasionally unexpected and sometimes violent reactions occur, even if the utmost caution in increasing the dose is exercised. It is possible that having obtained a certain degree of antitoxic immunity with a course of B. F., a secondary course in which B. E. is employed might prove more efficacious, and it is evident we have much yet to learn about the production of the tuberculous vaccines and their application in the treatment of disease. Time and experience alone can show us which tuberculin produces the best results, but thus far it has become apparent to me that whatever good results may be obtained depend quite as much upon the method used by the physician who administers the tuberculin as upon the kind of tuberculin he administers.

The method is of the utmost importance. We have seen that success or failure in attempts at immunization experimentally depends to a great extent on the method of immunization, and this must hold with even more force in trying to produce a certain degree of immunity in the individual already suffering from an infection. We have at present two methods to guide us in the use of tuberculin: the laboratory method and the clinical method. The laboratory method is that which has been put forward by Sir Almaroth Wright as the result of his discovery of opsonins, and relies solely on the readings of the opsonic index as a guide, both as to dose and to intervals between doses. What may be called the clinical method has been developed gradually from the experience of those using tuberculin, and by it the dose given, the interval between doses, the length of the treatment, and the ultimate dosage reached, are controlled entirely according to the clinical manifestations of the case and the effect of the injections on the patient's condition and symptoms.

Little experience has as yet been accumulated in the treatment of tuberculosis, especially pulmonary tuberculosis, by Dr. Wright's method of using bacterial vaccines, but excellent results are reported in localized tuberculosis. It is greatly to be desired that we may learn something from Dr. Wright's discovery that will place the treatment of tuberculosis by vaccines on a more definite and scientific basis, and show us with more exactitude when our injections are benefiting the patient and also when they may be doing him harm. Apart from the technical difficulties involved in taking the opsonic index of a large number of patients under treatment, the

great amount of labor, skill, and time necessary in following out such a procedure in each case, and the numerous sources of error which militate against accuracy, we will have to learn more definitely how reliable a criterion of immunity the degree of phagocytosis really is.

The production of opsonins, like that of agglutinins, precipitins, etc., is only part of the complicated mechanism of resistance put forth by the living organism, and its exact meaning as a criterion of immunity needs to be more definitely demonstrated. Although in a general way increased phagocytosis means increased immunity, we must remember that by itself this reaction does not necessarily imply that the system putting it forth is immune. The englobing of the bacilli does not necessarily mean their destruction. We find in guinea-pigs, for instance, that if tubercle bacilli are introduced into the peritoneal cavity they are taken up in large numbers by the polynuclear leukocytes and englobed, and yet these animals are most susceptible to tuberculosis, and the englobing of the bacilli does not in any way protect them against general infection.

The old clinical method, which was tried with such disastrous results in the earlier history of tuberculin treatment, was based on the production of pronounced local and general reactions which were thought essential to cure. These we know now to be harmful, and the avoidance of marked reactions and the production of tuberculin immunity are the main features of the new method. The clinical and laboratory methods are in perfect accord as to the efficiency of minute doses and the danger of over-dosage; but Dr. Wright's method takes no account of habituation by progression in dosage and the production of tuberculin immunity, and merely aims at keeping the patient's opsonic index as high as possible by suitable and properly spaced small injections of the same, or about the same, amounts of tuberculin indefinitely repeated.

The clinical method aims to carry the patient to large doses—doses one hundred, one thousand, ten thousand times larger than the commencing dose—namely, to produce tuberculin immunity while avoiding marked reactions or any disturbance of the patient's general health; this may be accomplished in most cases by beginning with minute amounts, increasing so gradually and at such intervals, and extending the treatment over as long a time as is necessary to accomplish the desired result, no matter how long that may be. The main difference in the two methods, therefore, is that of progression in dosage, and also, to a certain extent, the interval between the doses, which is much longer in Dr. Wright's method than by the usual clinical method; and the question resolves itself into this: Which is the most reliable guide to dosage—the opsonic index, or the clinical observation of the patient's condition and symptoms? And is the production of tuberculin immunity essential or not?

In favor of progression it may be said that whatever effect we may produce by simply repeating indefinitely the same small dose

which maintains the opsonic index above normal, by progression in dosage we certainly bring about in the infected organism a very self-evident and easily demonstrable change; a change which renders it unsusceptible to doses of tuberculin sometimes ten thousand times greater than the amount which at first would have produced marked evidence of intolerance and violent constitutional disturbance, an amount many times larger than the healthy individual can withstand. In bringing about tuberculin immunity have we depressed the opsonic index, produced long negative phases, and harmed the patient? or have we progressed so gradually as to avoid negative phases, and has the stimulation of the cells resulted in the formation of antitoxins or antibodies which protect the infected individual, at any rate against some of the evil influences of his infection?

The improvement in the patient's general condition and in all the symptoms which are the direct result of his chronic toxemia while being injected with increasing amounts of toxin, would point to the conclusion that whatever influence progression in dosage has on the opsonic index, it has a favorable influence on the patient's disease so long as it is administered within the limits of his power to respond to the increasing doses by the production of increasing amounts of antitoxic or protective substances.

Are we in future to disregard progression and antitoxic immunity and confine ourselves purely to raising the opsonic index by using repeatedly the same small doses at long intervals?

Even if we are not, it is to be hoped that Dr. Wright's work may teach us where the clinical method is at fault, and how to remedy its defects. Any physician who has used tuberculin therapeutically very soon learns that it is an agent powerful both for good and for evil; that he is working somewhat in the dark; that he may at times be giving too much and at times too little; and that he needs some more accurate method to guide him in regulating the doses and the intervals between injections. Even in the present state of our knowledge about tuberculin immunization, however, this much I think may be said: that though better results might be had if we possessed more accurate data as to what we are accomplishing through our treatment, nevertheless if the rules which experience has already taught us are carefully followed there is little or no danger from tuberculin treatment by the modern clinical method. It is the gross disregard of these rules which may bring about disaster and aggravate the patient's condition. The main object to be kept in view in tuberculin treatment by the clinical method is to produce as strong an immunity to tuberculin as possible, while frequently repeated, mild and hardly perceptible local reactions in the tuberculous foci are taking place, but without bringing about any general fever reactions, violent local reactions, or disturbing the patient's general health more than is absolutely unavoidable. Physicians who have continued the tuberculin treatment have all

tried to meet the indications I have just referred to in their own way and in the light of their own personal experience, and from their observations the present mild method has been gradually evolved.

In the therapeutic use of tuberculin it is best to have a certain formulated schedule by which the initial dose, the intervals between injections, the rate of progression, and the ultimate dose to be attained are distinctly laid down, this schedule to be literally followed so long as the patient shows no evidence of intolerance, but modified at once, as soon as he does, to suit the requirements of each case. Many patients can be carried from beginning to end of the treatment—a period which, when no reactions occur, usually takes about eight months—without any symptoms which call for any departure from the schedule laid down. If this were always so the treatment would be simplicity itself, but unfortunately in the majority of cases, at some period in the treatment, sometimes at the very beginning, sometimes at the middle, and sometimes even at the very last dose, symptoms of intolerance appear, and it is then that the physician requires certain definite rules to guide him in his conduct of the case, and these rules I will briefly touch upon.

Each physician modifies any schedule of dosage he may use according to his experience as he becomes more familiar with the effects of the powerful toxin he is employing. My own ideas as to certain rules have grown into convictions, or have little by little undergone changes as my experience grew. At first I formulated a schedule of dosage of my own, which, however, lacked definiteness; but of late I have adopted the plan of injections laid down by Denys, because it has seemed to me simple, definite, and, so far as I have used it, practical, and can be easily altered to meet the requirements of each case, though it is no doubt susceptible of improvement.

The first rule—one which practical experience has long ago taught me to be essential—is to begin with very small doses; much smaller doses than are usually advised. It we remember that the object of tuberculin treatment is to avoid constitutional disturbance and violent reactions which lead, especially if repeated, to tuberculin hypersusceptibility and aggravation of the patient's symptoms, we will soon realize that the best way to do this is to build up the tolerance to the toxin very gradually; in my experience, by following this rule, the number of cases which go through the whole treatment without marked reactions is increased. Our aim should also be to put off reactions as long as possible, because if a marked reaction occurs at the beginning of the treatment it is exceedingly difficult to habituate the patient to increase in the dosage, while later in the treatment, possibly owing to the partial immunization already produced, reactions are more rarely followed by evidence of prolonged intolerance. It has been amply demonstrated that tuberculin hypersusceptibility may be produced in cases in which the diagnosis had been made only by the tuberculin test, so that the one marked

reaction which the test had developed made the individual, slight as the disease was, for a long time so hypersusceptible to the toxin that it became exceedingly difficult to produce any tolerance when the treatment was begun.

We find also that reactions take place more readily at doses fixed between 0.1 milligram and 1 milligram than perhaps at any other stage. We should, therefore, begin sufficiently far down the scale to carry the patient through these doses without producing a reaction. For all these reasons it is essential to begin treatment with very small doses; that is, for afebrile cases, $\frac{1}{10000}$ milligram of filtrate B. F., or Koch's B. E. (liquid measure, not solid substance), or $\frac{1}{1000}$ milligram of old tuberculin. Denys makes use of eight solutions in giving B. F. No. 1 contains $\frac{1}{10000}$ milligram to each cubic centimeter. This is for febrile cases only. No. 2 contains $\frac{1}{1000}$ milligram to each cubic centimeter; No. 3, $\frac{1}{100}$; No. 4, $\frac{1}{10}$; No. 5, 1 milligram; No. 6, 10 milligrams; No. 7, 100 to each c.c., and No. 8 is pure filtrate. Now the increase in using these solutions is always by 1 decigram of each solution, which is convenient to measure and easy to remember. As 10 decigrams, or 1 c.c. of each solution is reached, the next solution, which is ten times stronger and in which 1 decigram represents the same dose as 1 c.c. of the preceding solution, is taken up and the increase is again by 0.1 of the new solution until 1 c.c. is given, when the next solution is taken up in the same way until the end of the treatment. Thus for ten doses the increase for each dose is by $\frac{1}{10000}$ milligram for ten doses; then by $\frac{1}{1000}$ for ten doses; then by $\frac{1}{100}$ for ten doses; then by $\frac{1}{10}$ for ten doses; then by 1 milligram for ten doses; then by 10 milligrams for ten doses; then by 100 milligrams, until 1 c.c. of the pure filtrate or old tuberculin is reached. The increase is by 0.1 of each solution, and as each solution is ten times stronger than the preceding, the progression in doses is ten times greater at the end of every ten doses. Certain details of the treatment may be gathered from the appended Charts I and II. Approximately the same plan may be followed in giving Bacillen-emulsion, provided it is remembered the doses referred to in the above schedule are liquid measure and not solid substance.

Dr. Brown has found that at the Adirondack Cottage Sanitarium reactions occur more frequently at the second or third injection of a new solution. This is not to be wondered at, as the increase in dose is ten times larger when a new solution is taken up. To obviate this, the progression for each solution can be by 0.5 decigram instead of 1 decigram for the first three doses; then by 1 decigram for the remaining doses in each solution, or, if time is to be considered, the amount taken off the first three or four doses can be added in suitable proportion to the last six or seven. Thus instead of increasing 0.1, 0.2, 0.3 and so on to 10 decigrams the increase may be 0.1, 0.15, 0.2, 0.25, 0.3, 0.4, 0.6, 0.8, 0.10. In truly apyretic

cases with good nutrition the physician in his discretion can make the increase for the first two solutions by 0.2 decigram, but after the dose of $\frac{1}{100}$ milligram is reached the increase for the remaining solutions should be 0.1 decigram of each solution.

The intervals between the injections are three or four days; generally two injections a week; but as the higher doses, such as 10 milligrams, are reached, the intervals may be five days, and after 100 milligrams six days, while the last three or four doses should be

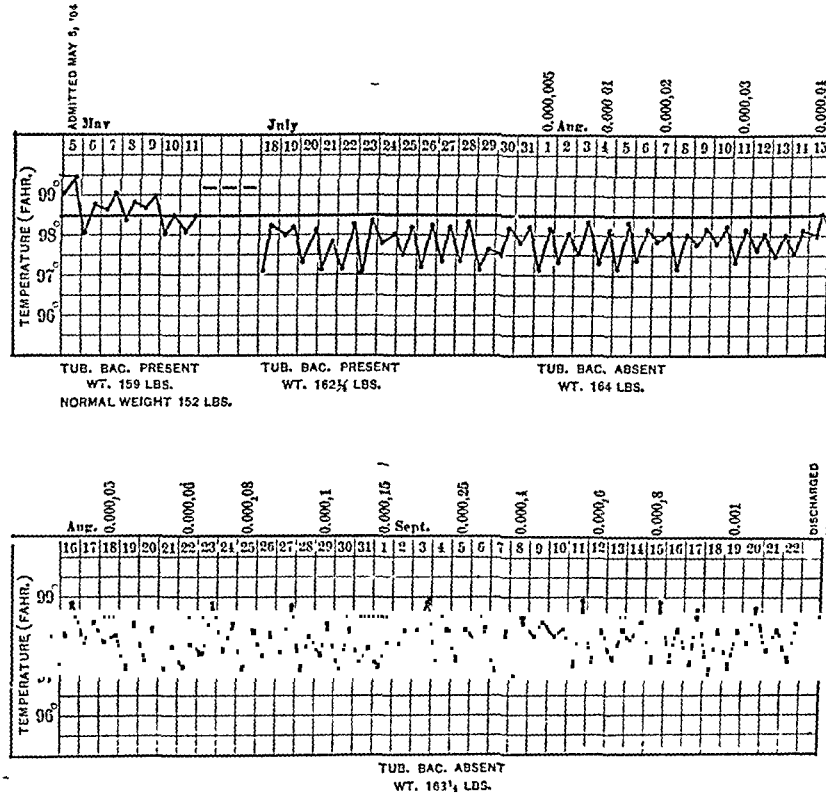

FIG. 1.—Details of tuberculin immunization.

given a week or ten days apart. Lowenstein finds that for Bacillen-emulsion longer intervals are necessary between the doses, especially when the large amounts are reached.

If no intolerance is manifested the treatment will require six months; but in the majority of cases when any reactions occur it should be extended over ten months or a year, or even much longer, if necessary, to reach full doses. It is a mistake to try to shorten the time by increasing the doses too rapidly, or decreasing the intervals. Whatever degree of immunity, antitoxic or otherwise, is produced by the treatment is produced only very gradually, and besides the risk to the patient which is always involved by haste, the intolerance it may produce takes often so long to overcome that

the duration of the treatment is lengthened rather than shortened in the end.

Tolerance to tuberculin is an excellent prognostic sign and it bears a certain relation to the condition of the patient's general

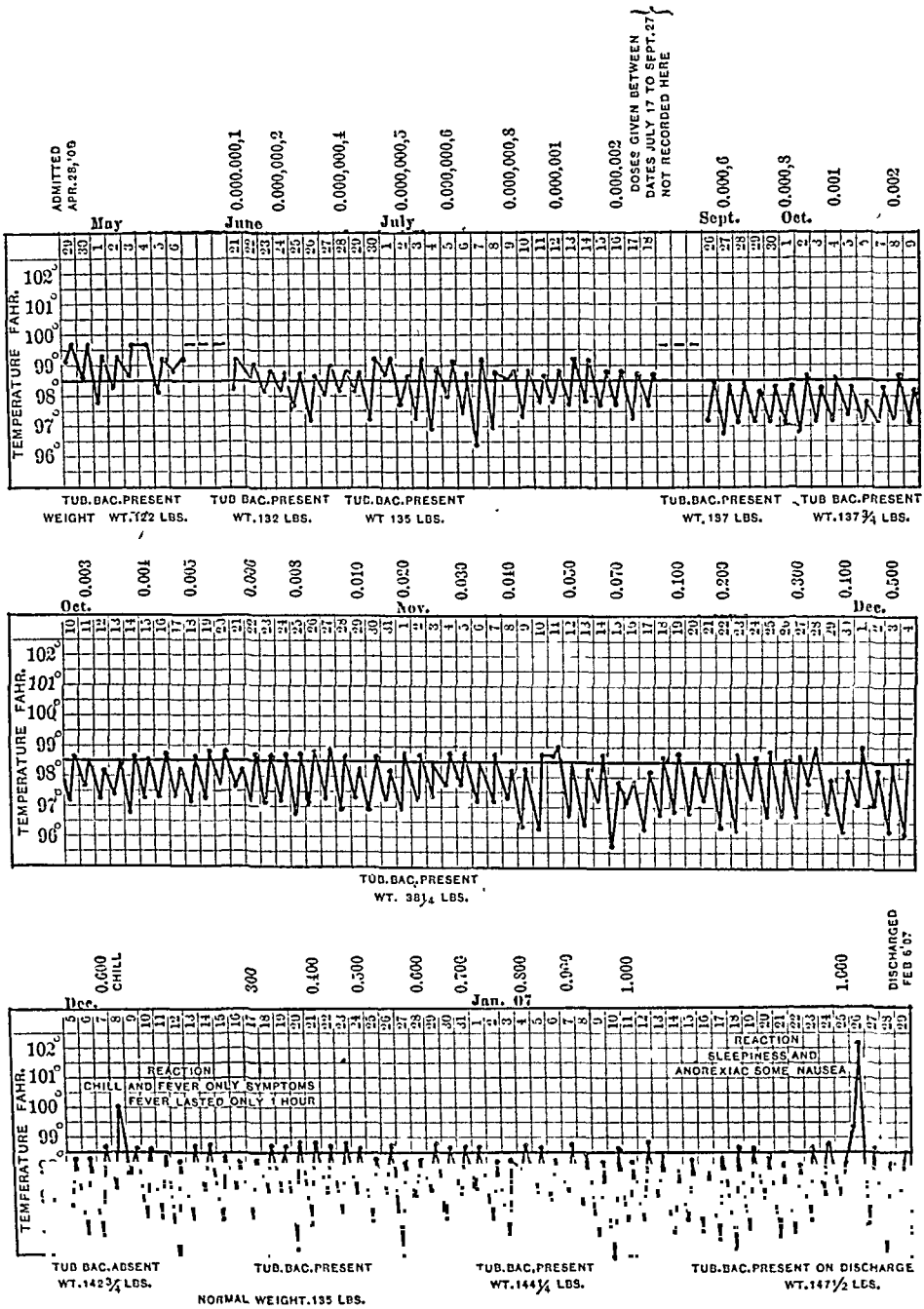

FIG. 2.—Details of tuberculin immunization.

health; and the more this improves the less apt is he to develop symptoms of prolonged intolerance, but the improvement in the general health is necessarily a slow process.

How does intolerance show itself, and how are we to proceed when it does? The symptoms of intolerance may be divided into three groups: those of a general fever reaction, those which indicate local reaction, both at the site of disease and also the site of injection, and those which point to general constitutional disturbance, as manifested by malaise, headache, sleeplessness, wandering pains, anorexia, nausea, and loss of weight and strength. Any one of these three groups of symptoms which constitute the fever reaction, the local reaction, or the constitutional impairment may be present separately, or some of the symptoms out of each group may show themselves; but they all, whether present separately or collectively, indicate intolerance and are to be considered before another injection is given, and in determining its strength when it is given.

The fever reactions are of two kinds: the short and the prolonged reaction. The short reaction is identical with that produced by the tuberculin test, and shows the classical fall and rise of temperature all ending in forty-eight hours; the prolonged reaction begins generally more gradually; the symptoms are mild; the fever rises less high but maintains itself, with a morning remission, above the patient's normal temperature range for several days, generally not more than a week. These prolonged reactions show the same temperature curve and all the other manifestations so commonly observed in the exacerbations of chronic pulmonary tuberculosis, except that usually they are of shorter duration. The temperature may not be more than 1° above the patient's usual range, or even less, but it does not fall for several days.

Local reaction at the site of the lesion is a valuable guide to dosage; increased cough and expectoration, pleuritic pains, aggravation of the physical signs, hoarseness, pain and aphonia if the larynx is involved, all point to local reaction and are all indications for caution in increasing the dosage. If moderate, they soon subside if the injections are discontinued for a short time or the dose lowered, and, no doubt, when moderate, local reactions are of benefit to the patient in bringing about reparative processes and in ridding the system of pus and septic material, for we have no better expectorant than tuberculin. In support of this view is the improvement in the patient's general condition and the marked diminution in the fever, cough, and expectoration which often follow moderate local reactions at the site of the lesions.

Local reaction at the site of injection shows itself by more or less extensive redness, œdema, and pain at the site of the injection; when slight, it may be disregarded, as it is somewhat influenced by the manner of injection or other causes; but if marked, it indicates commencing intolerance and should be considered in connection with the patient's other symptoms before increasing the dose.

Most important, and most often disregarded because no rise in temperature may be present, is the group of symptoms which point

to constitutional impairment resulting from overdosage. They are all the symptoms that chronic toxemia might be expected to produce, and all point to the supposition that the patient cannot respond by the formation of antitoxins and antibodies to the increasing doses of toxin which he is receiving. Even if no fever above the usual range be present, the patient who has been improving and whose general condition has been satisfactory, may show marked arrest in his improvement; if the injections are persisted in and the dose steadily increased, he will complain of malaise, exhaustion, headache, sleeplessness, wandering pains, anorexia, nausea, and loss of weight. If these symptoms are disregarded, the injections continued, and the dose heedlessly increased, in time the patient's disease may take on an acute form. When intolerance manifests itself, whether by general fever reactions, by evidence of local reactions, or by some of the symptoms of constitutional impairment, the rule is never to inject while any of these symptoms is still present, but to wait until the temperature has returned to its usual height, until the cough and increased expectoration have lessened, and all evidence of constitutional impairment, such as anorexia, malaise, debility, etc., have disappeared. Indeed, all evidences of intolerance must have been absent for at least two days before the injections are again taken up. When a febrile reaction has occurred, if the fever has been high or prolonged and the constitutional disturbance marked, the same dose that produced the disturbance should not be repeated, but should be decreased by one-half or more; if this produces no ill-effect the usual ratio of increase and intervals may be resumed until the dose which produced the reaction is accepted without disturbing the patient. If the reaction has been very mild the same dose which produced the symptoms may be repeated, but it is usually better to decrease the amount somewhat. In case local reactions at the site of injection or at the site of the lesions takes place without other symptoms, an interval of rest may be given and the same dose repeated. Sometimes it happens that there is no distinct fever reaction, no distinct local reaction, but as the doses are increased the patient begins to show some of the symptoms of constitutional impairment referred to; the same principle would apply here: discontinue injections until the unfavorable symptom or symptoms have disappeared, then begin again with greatly reduced doses, and increase gradually as heretofore. When in doubt as to the explanation of any slight symptom of intolerance, always omit one or two injections and then begin by repeating the last injection.

We have learned that "No reaction, no cure," has been a most misleading axiom, for we can have tuberculin immunity without reactions, and many reactions without any tuberculin immunity. Strong and frequent reactions are harmful, and yet while patients who go through the entire treatment without appreciable fever reactions derive all the benefit that could be expected from the treatment,

I have noticed that often when the patient's improvement seems at a standstill he will again begin to improve after he has had some evidence of a moderate local or even general reaction. The disturbance caused from the reaction having passed away, injections having been discontinued for a while and the dose reduced, the improvement in the general condition and symptoms seems to manifest itself anew when before it was at a standstill.

Tuberculin hypersusceptibility is an occasional complication in the course of tuberculin treatment which often takes infinite care and patience to overcome. By hypersusceptibility we do not mean the usual susceptibility to an increased dose which shows itself by an ordinary reaction, but an exaggerated and growing degree of sensitiveness to the toxin which often follows an ordinary reaction without any previous warning. For instance, a patient having reacted in the usual way to 1 mg., and all the symptoms of the reaction having disappeared and the temperature become normal for two days, an injection of 0.5 mg. is followed by a marked, even a more marked, disturbance than the one produced by the 1 mg. dose. Another interval of rest being given and the dose reduced to 0.1 mg., another strong fever reaction manifests itself, and this continued and sometimes increasing susceptibility of the organism to a decreasing dose of toxin constitutes tuberculin hypersusceptibility. Years ago I was accustomed to discontinue the treatment entirely in such cases, but it is not necessary to do so. All injections should be discontinued for ten days or two weeks and then resumed again, beginning far down the scale and increasing very gradually, according to the usual schedule. Thus, if 1 mg. has been the offending dose, go back to the $\frac{1}{100}$ mg. and follow the usual schedule of increase until the patient is carried safely by the dose to which he showed such peculiar and pronounced intolerance. By the clinical method, as briefly outlined, if time enough be allowed, tuberculin immunization may be carried often to full doses: 1 c.c. of old tuberculin, of B. F. or B. E., liquid measure, with safety to the patient, and often with a marked beneficial influence on his disease.

The two most important factors in obtaining results are the length of time over which the treatment is extended and the dose of toxin the patient can be made to tolerate. Whatever reparative changes in the lesions are brought about by the treatment are necessarily very slowly produced, and it would seem that any antitoxic or antibacterial immunity obtained is also slowly induced; its degree will necessarily depend to a great extent on the amount of tuberculin to which tolerance can be established. Not much permanent good can be expected from a short treatment extending over a few months, especially if a fraction of a milligram is the highest dose reached at the time the treatment is discontinued. On the other hand, when full doses have been reached they should not be continued indefinitely for fear of exhausting the patient's power to

respond, by the formation of antibodies, to the stimulus of the injection of toxin. It is well known that the horse's power to produce antitoxin can thus be exhausted, and when full doses can be reached, say 1 c.c. of the B. F., the O. T., or the B. E., no matter how long it may have taken, it is better to discontinue treatment for from three to six months and resume it again if anything in the patient's symptoms or condition seems to make it necessary.

In applying the tuberculin treatment in sanatoria the time required in most cases to attain the best results and to carry the patient to full doses is a serious objection, but it can be overcome by arranging with the patient's physician for a continuance of the injections at the patient's home, or for the application of a secondary course of injections after several months' rest when this is deemed advisable. This plan has been carried out already for some of the sanitarium patients by Dr. J. A. Miller. Whether tuberculin immunization is a strong enough influence for good to make it worth while to treat with it incipient and favorable chronic advanced cases in cities and without change in their mode of life, would be a most interesting study. I understand Dr. J. A. Miller, in New York, and Dr. Hawes, in Boston, are making a trial of the treatment under such conditions.

As to the type of cases suitable for tuberculin treatment, Denys and some of the Germans claim that even in acute cases good results may be occasionally expected by a careful course of injections, but my experience has been, with a very few exceptions, in treating patients who were apyretic or nearly so, that is, whose temperature rarely rose above 99.5° to 100°. The more chronic the type of disease the better adapted the case has seemed to me to tuberculin treatment, and most cases of a chronic type, whether incipient or of long standing and advanced, provided the nutrition is good and no serious complications exist, will derive more or less benefit from tuberculin immunization. The benefit derived may be from mere temporary improvement in all the symptoms to apparent restoration to health, with disappearance of bacilli often lasting for years. All acute cases, early cases in which the onset is acute, or advanced

complications, and patients who show pronounced and uncontrollable intolerance to tuberculin, are manifestly unsuitable for treatment.

The more familiar one becomes with the varying course of chronic tuberculosis, the easier it is to realize the difficulty of setting forth any positive evidence as to the favorable influence *per se* of any specific treatment when so many other factors influence the course of a disease, in itself so erratic and varying in its manifestations. The effect of tuberculin treatment on the patient is so gradual, and so slight are the apparent results, even for many months, that it is difficult to determine whether anything has been accomplished or not.

My own favorable impression of the influence of tuberculin has been principally formed by noticing how rarely the disease seemed to progress by the usual exacerbations and relapses in patients who were tolerating progressively increasing doses of tuberculin well, and in watching chronic cases who were running a slow but steadily downward course, in spite of the climatic and open-air treatment, derive marked benefit and even gradually return to apparent health after a full course of injections. It is especially in cases in which no marked intolerance to the injections has shown itself that one observes all the evidences of the chronic toxemia from which the patient suffers slowly disappear. The appetite, digestion, and nutrition all improve, the strength improves markedly, the slight accessions of temperature to 99° or 99.5° which may have been present, perhaps for years, from time to time, grow less and the temperature becomes practically normal. The subnormal morning temperature is less marked, the cough and expectoration which at certain periods in the treatment may have been increased gradually diminish, and in some cases entirely cease. In others, however, the patient may recover practically normal health, while the cough and expectoration persist apparently indefinitely, though much lessened. No marked influence on the bacilli is noted for many months in most cases. After local reactions the bacilli may greatly increase in numbers, to again decrease and occasionally disappear before the end of the treatment; but in many cases the bacilli may persist in the scanty sputum, though the patient may have regained apparent good health. In such patients, after an interval of rest, the repetition of the treatment is indicated, and a secondary course of injections is generally so well tolerated that the patient can be carried to full doses in three to four months. often without reactions.

Roemisch, of Arosa, has observed several such cases, in which after a short course of injections the bacilli entirely disappeared, and failed to reappear, though some sputum remained, which was examined negatively at intervals for as long a time as three years.

My belief in tuberculin immunization as favorably influencing the course of chronic tuberculosis rests on no more stable foundation

than a strong clinical impression gained many years ago—an impression which has gradually become a conviction through years of observation. I have no statistics to present beyond what the postdischarge mortality of the patients at the Sanitarium has shown: namely, that from 18 to 25 per cent. more of treated than of untreated cases discharged from the Sanitarium during the past fifteen years were living at the time we made the inquiry. A continued study of the postdischarge mortality, extending over sufficient cases and sufficient years to exclude sources of error from other influences, can alone in time furnish unquestionable evidence as to the exact value, if any, of tuberculin immunization in prolonging life. Sahli has aptly compared its influence in the treatment of tuberculosis to that of digitalis in the treatment of heart disease, while such an excellent authority as Meissen, in Germany, denies that it has any curative influence.

That tuberculin is not the vaunted and long-looked-for specific it was at first thought to be has been amply demonstrated by the bitter experience of the past. We have learned the dangers of tuberculin treatment and its evident limitations. We have, however, also in late years learned something about the complex defensive resources of the living organism which tend to the production of immunity, and how to call them into action, though we are evidently as yet only on the threshold of the knowledge of immunization by vaccines in the treatment of chronic infections. Everything we know, however, points to immunization as the goal toward which our efforts should be directed. We have much to learn about tuberculin treatment, but even in the present state of our knowledge I am inclined to think that the production of tuberculin immunity by the mild clinical method is capable of favorably influencing the course of chronic tuberculosis, of prolonging life, and in many cases of aborting a commencing infection or extinguishing the smouldering fires of a chronic infection.

CHRONIC POLYCYTHEMIA AND CYANOSIS WITH ENLARGED SPLEEN (VAQUEZ'S DISEASE).[1]

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The syndrome chronic polycythemia and cyanosis with enlargement of the spleen is held by most writers to be a distinct clinical entity. This symptom-complex was first described by Vaquez,[2]

[1] Read at a meeting of the College of Physicians of Philadelphia, April 3, 1907, and at a meeting of the Academy of Medicine, Cleveland, Ohio, March 15, 1907.

[2] Compt.-rend. Soc. de biol., 1892; Bull. Soc. des hôpitaux, 1899, p. 579.

who published a brief paper on the subject as early as 1892. It was discovered independently by Rendu and Widal[3] in association with primary tuberculosis of the spleen. More recently rather exhaustive studies of the subject have been undertaken by various observers and clinicians, more particularly Osler,[4] Türk,[5] Reckzeh,[6] Weber and Taylor, and others; and whilst these have somewhat increased our knowledge of the syndrome, quite divergent views are entertained relative to its nature and pathogenesis.

It should be understood at the outset that polycythemia, due to a deficiency in the plasma of the blood, a common condition attributable to a great variety of definite, ascertainable causes, such as acute diarrhœa, dysentery, cholera, and the like, should not be confused with true polycythemia with enlarged spleen of obscure origin. The abnormal increase in erythrocytes of congenital heart disease, valvular affections, adhesive pericarditis, obesity, a paralyzed extremity, and of high altitudes, in the opinion of most writers, likewise differ from the form under consideration. The hyperglobulism observed in ether anesthesia and phosphorus poisoning should also be excluded.

Etiology and Pathogenesis. At present writing it is believed by certain observers that stagnation of the blood due to a variety of factors is the sole cause of the symptom-complex. For example, in a case reported by Reckzeh, occurring in a young man, a malignant tumor of the thymus gland and lung caused gradual compression of the superior vena cava followed by polycythemia (limited, however, to that portion of the body which was affected by the venous obstruction), chronic cyanosis, and splenic enlargement. The lesson taught by the case in question was confirmed by experiments on two animals to the satisfaction of Reckzeh; he found that compression of the superior vena cava caused sufficient stagnation of the blood current to induce the development of a moderate polycythemia (6,200,000).

A. N. Hall[7] suggests that the polycythemia may be a compensatory process—an attempt to make up the deficiency in oxygen-carrying capacity of the individual cells by an increase in the number of cells. Moreover, polycythemia and enlargement of the spleen has been observed in obstructive cardiac lesions. Thus E. Weil[8] found red transformation of the bone-marrow (the normal fatty tissue having disappeared) in postmortem examinations on two children with congenital pulmonary stenosis and chronic cyanosis. As stated above, most writers contend that polycythemia and enlarged spleen is a condition which is not synonymous with chronic cyanosis due to chronic valvulitis.

[3] Bull. et mém. Soc. des hôpitaux, 1899, III Ser., p. 528
[4] Trans. Assoc. Amer. Phys., 1903, p. 316
[5] Wien. klin. Woch., 1904, Nr. 6 u. 7.
[6] Ztschr. f. klin. Med., 1905, lvii, 215.
[7] Amer. Med., June 27, 1903.
[8] Compt.-rend. Soc. de biol., 1901.

It can be readily understood how an unequal distribution can show polycythemia on examining the peripheral blood. It is a recognized fact that local cyanosis from any cause calls forth an increase in the number of red cells. It would appear, therefore, that any condition accompanied with cyanosis should be capable of inducing polycythemia.

On the other hand, it has been claimed that polyglobulism is ascribable to an overproduction of erythrocytes as a primary change, and this view is supported by the necropsy findings of a case reported by Weber and Watson:[9] they had convincing evidence that an increased production of erythrocytes was taking place in the bone-marrow. These observers, then, are inclined to regard the changes in the bone-marrow as primary, or, if not strictly speaking *primary, as representing an excessive "vital reaction" to stimulating agents.*

Weber and Watson account for the symptom-complex of the condition on the supposition that the osmotic tension of the blood of patients with extreme polycythemia is higher than that of ordinary blood. Bence[10] holds the syndrome to be primarily due to an overproduction of red cells; he argues that the qualitative change in the various anatomical elements of the blood point to increased erythroblastic activity of the bone-marrow. Widal, assuming tuberculosis of the spleen to be a uniform pathological finding, thinks the diminished function of that organ produces increased activity of the bone-marrow.

Türk believes it to be a primary affection of the bone-marrow. Rosengart[11] found evidence of hyperplasia of the leukocytic myeloid tissue, including mast cells, myelocytes, and erythroblasts, in the spleen and liver. In one case this observation led Türk[12] to suggest that the syndrome was dependent on hyperplasia of this erythroblastic myeloid tissue plus the histological changes noted in the liver and spleen by Rosengart, a condition analogous to the hyperplasia of leukocytic myeloid tissue in myelogenous leukemia.

These changes, however, have not been noted by other observers. A. V. Korauspi[13] argues that the deficiency of carbon dioxide in the blood demands an increased hemoglobin content, hence also a polycythemia to maintain the normal acidity of this tissue. Limbrea first pointed out that polyglobulism goes hand in hand with carbon monoxide poisoning. Julius Bence found experimentally that the inhalation of carbon monoxide decreased the erythrocyte count from 9,860,000 to 8,000,000 and a simultaneous, distinct falling off in the viscosity was noted. He regards the fact that the inhala-

[9] International Clinics, 1905, vol. iv, 14th series, p. 47.
[10] Deut. med. Woch., 1906, xxxii, Nr. 37.
[11] Mitteil. aus den Grenzgeb. der Med. und Chir., 1903, iv, 495.
[12] Wien. med. Woch., 1902, Nr. 5, p. 226
[13] Quoted by Bence, Deut. med. Woch., September 13, 1906.

tion of carbon monoxide produces a rapid reduction of the erythrocytes in these cases as prima facie evidence that the polycythemia is the result of a diminished percentage of this gas in the circulating blood.

Among the earlier reports of cases, principally by French writers, tuberculosis of the spleen was noted. But cases of splenic tuberculosis have been known to occur without polycythemia and cyanosis. For example, Reckzeh reports a fatal instance of tuberculosis of this organ, as shown clearly by an autopsy in which the characteristic features of polycythemia and cyanosis failed to appear during the life of the patient. Türk also reports two of his own cases, and four additional cases from the literature, in which tuberculosis of the spleen was wanting. It is quite certain that whilst the association of splenic tuberculosis with polycythemia and cyanosis is sometimes met with, the latter may occur without he presence of the former.

My observations in Case I, reported below, leads me to the conviction that defective venous tonus plays an important role in the pathogenesis of the condition. The nervous phenomena are at times, at least, well-marked and peculiarly distressing, as shown by the history of one of the subjoined cases.

CASE I.—A. W., female, single, aged twenty-five years; height 5 feet 6 inches; weight 198½ pounds; was referred to me by Dr. Finney, of Baltimore. First came under observation September 23, 1904. The family history showed Bright's disease among the mother's antecedents; also eczema, rheumatism, and cases of moderate obesity. The mother, however, is living and in vigorous health; the father is deceased, of organic heart disease complicated with chronic nephritis, at the age of forty-two years. One brother was a hemophiliac; otherwise the family history was unimportant.

The patient had not contracted any of the usual childish diseases except measles at twelve years of age, at which time she arrived at puberty. Later she suffered from colds in the head, with much catarrhal discharge. At seventeen years of age she had congestion of the lungs, and the eyes had been bad for fifteen years. From the eleventh to the twenty-third year of age the patient experienced one or two attacks of nose-bleed each month. Menstruation was formerly painful, but not now; it is irregular, however, recurring every two or three months, and consisting of a dark-brown discharge. Patient has pursued active physical exercise and has dieted with a view to reducing the bodily weight, but without results. Cyanosis, which had slowly increased, was first observed ten years since.

Miss W. has been inclined to rheumatism for eight years, and subject to severe headaches during the same period. For one year prior to her first visit (September 23, 1904) the headaches had improved, but the cyanosis had become worse; at the same time she

also suffered from violent cramps in the legs and feet. At the date of her visit the mucous surfaces were somewhat less livid than the skin. For several years the patient has been timid, mentally distressed, and apprehensive to a degree. She complained of slight vertigo at intervals. The urine analysis proved negative, as a rule, in its results. On one occasion, however, a reaction for sugar was obtained, the percentage being less than one.

A blood examination on four different occasions gave the following average result: red cells ranged from 5,300,000 to 6,960,000. The hemoglobin value averaged 110 per cent., while the leukocytes varied from 13,600 to 20,000. The red cells are overburdened with hemoglobin; they stain about normally and are of natural size and form. The white cells show mostly polymorphonuclear elements.

Physical Examination. The patient is a well-developed female subject, with good musculature and prominent panniculus adiposus. The face is markedly cyanotic, presenting a livid-red appearance everywhere except around the mouth, chin, base of the ears, and a narrow border around both eyes, the latter areas looking blanched by contrast. Both cheeks and forehead show a far greater degree of cyanosis than the rubicund face of plethoric obesity. As in other cases reported, pressure upon the skin left a decided anemia, which slowly became effaced. Examination of the superficial veins of the face conveyed the impression that they were greatly lacking in tonicity. The apex beat is indefinable, owing to corpulency. An examination of the lungs proved negative in its results. The heart shows slight enlargement of the left ventricle. It is difficult to delimit the organ, however, owing to the subcutaneous fat deposits. The first sound is somewhat muffled, the second aortic slightly accentuated, and the action of the heart is abnormally rapid, the pulse ranging from 110 to 120. There is no evidence of arteriosclerosis and the blood pressure tested by the Riva Rocci blood-pressure instrument—systolic 145, diastolic 115. The spleen is found to be slightly enlarged. The liver is of normal dimensions; also the thyroid gland. No other abnormal physical signs are discoverable.

The treatment was directed toward the reëstablishment of the menstrual function, and after eighteen months the menses occurred every six weeks. The patient has been seen at intervals of two or three months from the date of my first examination until the present, and the course of the complaint has been marked by recurring exacerbations and remissions. The headaches, however, have been practically absent for a year or longer, or since the menses have been more nearly normal; the distressing feeling of apprehension has also undergone noticeable improvement, particularly during the last six months, and the same is true of the cyanosis. At date of writing (January 20, 1907) the nervous tremor, mental apprehension, and the endurance show marked improvement. It is worthy of note

that the nitrites afforded considerable temporary relief from the headaches from the beginning, thus showing that the cause of the headaches most probably was in part at least heightened tension in the cerebral vessels.

CASE II.—A male, aged thirty-one years, a clerk; height 5 feet 9 inches; weight 125 pounds; came under my care June 7, 1904. The mother died of childbirth at forty-five years of age. The father is living and healthy. He has brothers and sisters, all of whom enjoy good health. The previous diseases from which the patient suffered were mumps, whooping-cough, and two attacks of influenza in adult life; he has also been susceptible to "colds" in the head and chest, which he ascribes to catarrh of the naso-pharynx.

The social history shows moderate indulgence in tobacco and alcohol, the free use of coffee, rarely tea, and the usual indifference to diet. There is no history of either gonorrhœa or syphilis. The patient is married and has three children, all healthy. He has complained of indigestion at intervals for the past fifteen years, the principal symptoms being fulness, eructation of gas, and discomfort in epigastrium, shortly after the ingestion of food; the bowels act regularly; the vision is blurred at times, and headaches, mental apprehension, and slight dizziness have been the chief nervous phenomena; for several years the patient has become easily fatigued on muscular exertion (asthenia); the legs are weak and also the grasp; he sleeps well; during the day he has considerable cough attended by mucoid expectoration and thoracic pains, which radiate to the lumbar regions.

The *physical examination* shows at a glance cyanotic lips, conjunctivas, ears and face (especially the nose); the hands and feet are also quite dusky. This cyanosis had been present for five years. The left ventricle is somewhat enlarged (hypertrophied), a faint systolic murmur is heard at the apex, and the second pulmonary sound is moderately accentuated. The spleen is palpable; but not markedly enlarged. The pulse is somewhat accelerated, but the tension is not abnormally high. The urine contained no albumin. A blood examination by Dr. Batroff showed: red cells, 7,400,000; leukocytes, 12,600; hemoglobin, 130 per cent.; color index 0.88 per cent. The differential count gave this result: polymorphonuclear leukocytes, 69.30; small lymphocytes, 23.72; large lymphocytes, 6.5; eosinophiles, 0.5 per cent.; absence of poikilocytes, macrocytes, microcytes, and nucleated red cells. The red cells were of uniform diameter, and contour was perfectly preserved; no crenation or other abnormality, and the staining capacity exceedingly good.

The patient has been seen at long intervals until the present time. The principal complaint at these visits was nervous apprehension, momentary dizziness, and disinclination for exertion, either mental or physical. As the result of treatment, chiefly dietetic,

the digestive function has been improved, but the cyanosis and nervous phenomena have been only slightly relieved, if at all. Small doses of cardiac stimulants, such as digitalis and strychnine, seemed to afford relief from the cyanosis and increase the general strength, but only temporarily. The nitrites also failed to bring about lasting improvement, although affording some degree of relief from the cerebral symptoms.

CASE III.—A third case, in which the diagnosis may be questioned on some accounts, came under my notice September 23, 1904, through the kindness of Dr. Prickitt, of Mt. Holly. The history is as follows:

E. A., aged twenty-one years; single; height 5 feet 3 inches; weight 86 pounds. The father is deceased, from necrosis of the leg following an operation; the mother lives and is healthy; has two brothers and two sisters who enjoy good health. Apart from neuropathic heredity on the mother's side, the family history is of no etiological importance.

Patient experienced the usual childish diseases, and at twelve years of age developed chills, accompanied with fever and sweats, (presumable malaria) lasting several weeks. Later, or when seventeen years of age, was operated on for appendicitis (primary attack); at the age of nineteen years received a blow by a hard ball over the right ovary. This was followed by inflammation and three abscesses which ruptured into the uterus; cystitis followed, and two years later, May, 1905, curettement was performed; subsequently acute nephritis developed. The menstruation began at eleven years, has been somewhat painful, and since the operation for appendicitis has shown a markedly irregular tendency.

The present illness dates from the operation for appendicitis, four years ago, although no cyanosis developed until after the curettement in May, 1905. The urine is scanty, dark, alkaline in reaction, and slightly albuminous; no casts are present. Physical exertion increases the cyanosis and induces dyspnœa. The patient is weak and neurasthenic.

The skin is markedly livid, especially that of the face, and there is obvious inspiratory dyspnœa; the pulse is rapid, small, and compressible, and the heart slightly dilated, and an occasional systolic murmur is audible at the tricuspid orifice. The abdominal walls are tense and hard to the feel; no splenic enlargement is detectable, and there is no œdema of the lower extremities.

The blood examination by L. N. Boston shows a cyanosed condition of this tissue; blood flow from puncture free; hemoglobin, 120 per cent.; erythrocytes, 4,290,000; leukocytes, 11,100. The stained specimen reveals many poikilocytes, a few macrocytes, and some nucleated red cells; all cells overstained and very deeply. A subsequent blood examination (made by W. C. Batroff) gave a somewhat different result: the blood flows freely from puncture,

and resembles chocolate in appearance; the hemoglobin value from a cyanosed finger is 79 per cent., from a cyanosed ear 110 per cent.; red cells 4,800,000, white cells 8400; differential count of leukocytes shows: polymorphonuclear 67 per cent., small lymphocytes 24 per cent., large lymphocytes 7 per cent., eosinophiles 1 per cent., mast cells 1 per cent. The corpuscles are generally large, with decoloration of the centres; a few poikilocytes, few macrocytes, but no erythroblasts were found.

In this case the structure of the blood is somewhat abnormal, and while the color index shows no anemia present, but rather the reverse, the red-cell count (4,290,000 to 4,800,000) is comparatively low, and there are abnormalities in form and size of the corpuscles. It scarcely seems tenable to suppose that the principal difficulty in this case consists in deficient oxidation, owing to the absence of an increase of the red corpuscles, to account for the excessive hemoglobin content of the erythrocytes. A tabular record of my own and all the cases not included in Reckzeh's list is herewith appended:

TABLE I.

Case	Author	Sex, age	Splenic enlarg.	Albuminuria.	Hemorrhage.	Result	Remarks
1	Weber	F. 37	Yes	No	No	Improved	Absence of cyanosis
2	Zimlick	M. 32	...	No	No	Died	
3	Collins	F. 24	...	No	No		
4	Hall	F. 61	No	0.05%			
5	"	F. 40	No				
6	Weber and Watson	M. 58	Yes	0.5%	Hematemesis (?) 5 yrs. ago	Died	Cause of death, syncope
7	Engelbach and Brown	F. 40	Yes	Trace	No	No change	Duration 11 yrs.
8	Bence	M. 43	Yes	1%	No	"	No apparent obstruction after 5 yrs., but 9 yrs. cyanosis
9	"	F. 45	Yes	No	....	"	Short period. Began 2 yrs. ago
10	"	F. 42	Yes	No	....	"	Began 2 yrs. ago from gums bleeding
11	Koranyi[1]						
12	Hutchinson and Miller	M. 45	Yes	Trace	Yes	Died	Died of coma and hyperpyrexia. Duration 7 yrs. 2 mos.
13	Begg and Bullmore	F. 47	Yes	No	....	Improved	
14	Lommel	M. 42	Yes				
15	Robertson	M. 48	Yes	0.7%	Yes	....	Obstinate constipation
16	Aldrich and Crummer	F. 53	Yes	No	No		
17	Reissmann	F. 18	No	...	Yes	....	Signs of venous obstruction in chest and legs
18	Anders	F. 25	Yes	None	Yes	Improved	
19	"	M. 31	Yes	...	....	....	Began 10 yrs. ago

Remarks. My own figures coupled with those of Reckzeh (not included in my tables) give a grand total of 53 cases. These will form the subject of a few observations and inferences.

[1] No details. Case referred to by Dr. Bence. Treated with oxygen inhalations

TABLE II.—BLOOD EXAMINATIONS.

Author.	Erythrocytes.	Size and form.	Normoblasts.	Polychromatophiles.	Leukocytes.	Lymphocytes.	Leukocytes, mononuclear and transitional.	Polymorphonuclear.	Eosinophiles.	Mast cells.	Myelocytes.	Hemoglobin. %
Bence, Case I	10,340,000 9,440,000	Practically normal	1 1	None "	12,500 6,400	9.2 12.3	1.7 mono. ..	80.0 78.6	6.7 4.6	3.1	...	180 (Gowers)
" " II	8,000,000	....	..	..	....	....	..	....	....	....	...	27.2
" " III	8,350,000	....	..	.	8,400	....	..	....	....	....	...	27.8
Engelbach & Brown	10,909,000	....	..	..	9,600 (9 to 11%)	....	5.0 mono.	....	....	....	...	above 120
	8,037,000	....	..	Few	6,600	11.0 to 14.0	6.0 trans.	75.0 to 76.0	1.0 to 1.5	not increased		
	12,584,000	....	..		9,600							
Zimlich	6,480,000	....	..	..	13,200	12.0	5.0	85.0	2.5	....	...	120+
Ascoli	9,240,000 ?	....	..	..	 15,000	16.0	11.0	51.0	20.0	2.0	...	120+ 95, was 110
Weber	8,240,000	....	..	..	4,000	17.25	8.5	66.8	0.5	1.0	...	120
	10,960,000	....	..	..	9,000			81.0				185
Hall, Case I	9,949,600	Normal	..	..	6,500	....	..	....	....	....	...	170
" " II	9,935,000	....	..	..	22,000	....	..	....	....	....	...	200
Collins	9,821,000	Normal	..	..	17,800	26.0	..	73.0	0.5	....	None	160-170 110
Weber & Watson	10,000,000	Practically	..	..	7,500	17.4	..	82.4	0.2	....	None	170
	11,000,000	normal	..	..	8,000							
Koranyi {quoted by Benco}	7,400,000											
Hutchinson & Miller	8,000,000	Nothing	..	..	....	5.6	2.4	82.8	2.8	2.4	...	110
	11,000,000	abnormal	..	..	17,160							120
Begg & Bullmore	6,850,000	....	..	..	11,300	13.8	4.0	77.3	1.5	....	...	100
Lommell	8,230,000	....	..	None	11,000							
Aldrich & Crummer	7,700,000	Variation in size and contour	..	..	4,700	19	..	72.5	4.0	....	4.5	120
	6,048,000		..	..	5,500							90
Anders, Case I	5,300,000	Natural, overburdened with hemoglobin	..	..	22,000	38.05	.	61.9	0.5	....	...	110
	5,960,000		..	..	1,320,000							110
" " II	7,400,000	Normal	..	..	12,600	29.77	..	69.3	0.5	....	...	130 color index 0.88%

Sex. According to most writers, males are more prone to the affection than females, but of the 18 cases that I have collected, in which the sex is given, 11 (or 61 per cent.) were in females, and 7 (or 39 per cent.) were in males. Engelbach and Brown state that an "analysis of all the cases shows it to be about equally divided between the sexes."

Race. Of 7 cases reported by Türk, 5 occurred in Hebrews, and racial predisposition is generally conceded. Precise figures to indicate the influence of race, however, are wanting.

Age. According to Reckzeh, the great majority of the cases occur in the middle period of life. On the other hand, Türk's figures (based on a total of 20 cases) show that it occurs principally in adults. In my group of 18 instances the age was recorded, and of these 3 occurred between twenty and thirty, 3 between thirty and forty, 9 between forty and fifty, and only 3 after fifty years of age. My results, therefore, are in consonance with Reckzeh's, rather than with those of Türk.

Spleen. Reckzeh has pointed out that in only 2 (Osler, Cabot) out of 34 cases was there an absence of splenic enlargement. Of the 18 cases recorded in my table, splenic tumor occurred in 14, or 78 per cent. It was present in 44 out of a total of 49 cases collected from various sources by me, or in 89.8 per cent.

Albuminuria. This was present in 43 per cent. of the cases in my series in which the symptom had been investigated. Engelbach and Brown state that albuminuria occurs in one-half of the cases, in some in large amounts.

The most characteristic blood-finding is polycythemia. It has been held by certain writers that an erythrocyte count of less than 8,000,000 does not constitute polycythemia with enlargement of the spleen. On the other hand, Cabot holds that the red cells number about 7,000,000 in a typical case. Unquestionably, cases which presented every other characteristic clinical feature have been reported in which the erythrocyte count was below these figures. In Case III of my series (not included in my table) the erythrocyte count was only slightly above normal, if we regard 4,500,000 as the normal standard in the female. In the majority of instances, however, the red cells number over 8,000,000, as may be seen from a glance at Table II.

In most cases of polycythemia a moderate leukocytosis is present, although a few have been reported in which a leukopenia was found.

Cases have been reported in which the leukocyte count fell short of that of the erythrocytes. Thus in a case recorded by Osler only 4000 leukocytes per c.mm. were noted, while the red cells numbered 9,953,000; hemoglobin 120 per cent. On the other hand, we see in certain reported cases an increase of the leukocytes out of ratio to the erythrocyte count. For example, in some cases in which

the red cells did not exceed 7,000,000, the white cells amounted to over 20,000. The cases just related belong to this category. I mention these facts with a view to emphasizing the point that mere obstruction to the circulation, or blood stasis, does not account for this symptomatic manifestation.

Of 18 cases in which the leukocyte count is given in my table, 14 showed an increased number of leukocytes. Attention has been directed to a disproportionate increase in the polymorphonuclear leukocytes as an evidence of primary disturbance of the blood-forming organs. This finding, however, did not obtain in my 2 cases, and the table indicates the following in this respect: 7 cases in which the polymorphonuclear elements were relatively increased, and 7 cases giving a ratio at or below the normal. It would seem that the normal proportion of the different forms of white cells is maintained, as shown by the differential count, in about one-half of the cases at least. Analyzed with regard to the hemoglobin percentage, an examination of Table II will show that of 16 cases in which this percentage is reported 10 are above 120 per cent., 1 shows only 90 per cent., and another 100 per cent. In 1 of Hall's cases the hemoglobin value was 200 per cent.

Is the abnormal blood-forming power a physiological or a pathological process? It is clear that on account of the increase in the value of the various elements of the blood, which increase is usually more or less proportional, the blood-generating organs are stimulated, but the question arises, Is this a primary or a secondary role? Vaquez was the first to suggest that primary tuberculosis of the spleen was the cause of the syndrome. Bence, Widal, Türk, Osler, Rosengart, and Weber and Watson, previously named, all contend for a form of polycythemia with splenic enlargement, either of unknown etiology (Osler) or due to splenic tuberculosis or to a primary overproduction of erythrocytes from some stimulating agency not as yet discovered. As pointed out by Engelbach and Brown, and others, however, many cases have more recently come to autopsy, in which neither the spleen nor any other organs showed tuberculous lesions; hence this morbid process cannot be held responsible for all cases. In my cases and in many reported by other observers the blood examination failed to show changes in this tissue of sufficient importance to justify the inference that the blood-making organs are directly affected. W. Egbert Robertson informs me that in his case (Table I) no primary disease of the hematopoietic organs was indicated by the microscopic findings, the blood having been, on one occasion, taken from the spleen notwithstanding.

At present the balance of testimony is clearly in favor of the view that in many cases described as polycythemia and cyanosis with splenic enlargement, the extraordinary blood-making power, as shown by the increased number of red cells in the bone-marrow, is

probably secondary or physiological and quite analogous to what is sometimes seen after excessive hemorrhage.

In this connection certain well-established effects of venous hyperemia, due to some form of obstruction, should be briefly presented. In the first place, the velocity of the blood current is decreased in stasis, and although more than the usual number of corpuscles occupy the capillaries and veins, the temperature is low as compared with that of a part or parts of the body the seat of arterial congestion. As venous congestion advances with slow increase in the size of the veins and capillaries, the metabolic processes are profoundly affected and lowered, rendering the tissues abnormally susceptible to the influence of microbic and all other forms of irritants.

The cyanotic induration of the various viscera (liver, spleen, kidney) in consequence of continuous venous hyperemia is well known. Here the supporting structure of the organs is strengthened by the formation of fibrous tissue. Now, it is reasonable to suppose that analogous changes occur in the nervous structures, parts of the brain, spinal cord, ganglia, and nerve shafts that are endowed with connective tissue. We may assume that all tissues which are the seat of prolonged venous engorgement present pathological changes which are far-reaching and variable in character. The query here arises, Can we ascribe the nervous phenomena observed in chronic polycythemia and cyanosis with enlarged spleen to the effects of the venous obstruction? It is a matter of common observation that in chronic valvulitis the principal nervous features arise after failure of compenstion, or at a time when engorgement of the veins is present. When the left ventricle fails to maintain the movement of the blood in the capillaries (*e. g.*, in aortic incompetency), insomnia, headache, vertigo, restlessness, and weariness are observed. Again, emotion may induce palpitation. These symptoms all have their parallel in cases of chronic polycythemia with cyanosis, and the same is even more true of that prominent symptom, dyspnœa on muscular exertion. The comparison also holds, although less completely, with reference to the general neurasthenic symptoms.

In cases of true polycythemia and cyanosis with enlarged spleen there is a painful nervous apprehension, such as is witnessed in functional diseases of the heart arising from conditions outside of this organ. Every clinician of wide experience, however, must have met with structural affections of the heart in which the nervous equilibrium is more or less disturbed by this class of phenomena, *e. g.*, when the heart muscle is hyperesthetic from exhaustion.

The symptomatology of the condition, so far as observed, may be accounted for, in great part at least, by the persistent cyanosis, and the polycythemia may be looked upon as a result of the venous stasis; and this hyperglobulism is intended to compensate for the diminished oxygen-carrying capacity of the blood.

As stated above, however, true polycythemia and cyanosis with enlargement of the spleen, according to the majority of writers, exhibits a wider range of symptoms, as a rule, the nervous phenomena being especially conspicuous in the clinical picture, and the blood findings recorded in some cases, it has been justly claimed, are at variance with those found in mere stagnation.

It may be argued that if stagnation alone were the cause, the syndrome would probably show greater prevalence than it has done. Again, the cases would naturally subdivide themselves into local and general polycythemia according to the character and location of the vessels. I regard it as probable that there is a form of primary polycythemia of unknown etiology, characterized principally by marked polyglobulism and other hemic features, cyanosis, headache, vertigo, and splenic enlargement; but it must be of rare occurrence, while it is clear that the majority of the cases which have been reported and classed as instances of this condition have had a different pathological etiology, although closely simulating the primary variety clinically. Finally further proof, both clinical and pathological, is required before any of the theories thus far advanced can be accepted.

TREATMENT. As regards treatment, it may be said that no special methods thus far advanced have been accepted as generally applicable. The environment is to be made as favorable as possible physically and mentally. A light, nutritious diet, an abundance of fresh air and gentle methodical exercise, should be advised and encouraged. Of medicines, the nitrites have been most extensively employed, and they have afforded relief to the headache and other cerebral symptoms in some cases at least. As stated by Watson, venesection with or without the injection of saline, has been followed only by temporary effects. Begg met with a case, presumably of malarial origin, in which the vigorous treatment adopted in the East in such instances was resorted to, viz., the tri-iodide of mercury ointment was applied over the spleen, and the part exposed to artificial heat, while quinine was given in increasing doses up to 45 grains a day. As the result of this treatment, the few pathological elements shown by the blood examination progressively diminished; the spleen, which was enlarged, retracted upward two inches in the mammary line. That the principal benefit in Begg's case arose from the massive doses of quinine was shown by the fact that the temporary discontinuance of the remedy was followed by an increase in the size of the spleen. The results obtained in this case also point to a possible malarial origin of chronic polycythemia and cyanosis with enlarged spleen, in some instances at least. If this view be accepted, it is obvious that the blood changes presented by the syndrome in such cases are to be classified as secondary.

The viscosity of the blood is greatly increased in this condition, as shown by Weber and Watson; hence, on rational grounds, the use

of iodides should be advised. In my cases, however, their exhibition was without obvious beneficial effects. In Case I of my series, in which amenorrhœa and moderate obesity were present, improvement was noted on the reëstablishment of the function of menstruation.

THE PROGNOSIS OF TRANSIENT SPONTANEOUS GLYCOSURIA, AND ITS RELATION TO ALIMENTARY GLYCOSURIA.

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There are few diseases of metabolism about whose beginning less is known than that of diabetes, and the gratifying results so often obtained from prompt and intelligent treatment, even in advanced stages, make this obscurity of inception the more regrettable. We possess definite knowledge of the commencement of that very small group of diabetic cases following traumatism or disease of the nervous system, and of that group following or accompanying obesity, but of the early stages of the ordinary form, embracing the great majority of cases, we know very little. The few reported cases which have been followed from the beginning have shown at first either spontaneous glycosuria under ordinary normal conditions, or an alimentary glycosuria following ingestion of glucose, and later have gradually developed constant glycosuria and diabetes.

A preliminary consideration of the nomenclature will be of some help in understanding the discussion of our subject. The term transient or intermittent glycosuria is a very broad one, and includes practically all non-diabetic glycosurias, for all continuous glycosurias are diabetic. The adjectives used to describe the various glycosurias have, generally, some reference to their etiology; thus hepatogenous, that form arising from any disease or injury which causes the liver to discharge rapidly its glycogen; neurogenous, that form resulting from disease or injury of the nervous system (probably to be included under the previous variety); and alimentary, that form arising from the ingestion of carbohydrate food, etc.

Alimentary glycosuria, when arising from intake of any sugar, is termed *e saccharo;* when from starch, *ex amylo* (invariably diabetic); and when from a mixed diet, spontaneous. Spontaneous glycosuria may be transient or permanent, and if the latter is, of course, diabetic. The transient spontaneous glycosuria includes those cases in which we can rule out the other various causes of glycosuria, but of which we do not know the primary cause. The secondary cause, of course,

is inability to assimilate the starch and sugar of a mixed diet, but whether ultimately this is to be attributed to some transient disturbances of metabolism or to a beginning diabetes, we do not know. The usual term for this glycosuria is simply transient or intermittent, but transient spontaneous seems a more suitable term, and we shall use it to designate those transient glycosurias of unknown origin appearing on an ordinary mixed diet. The part transient disturbances of the pancreas play in the production of many of these non-diabetic glycosurias is yet to be definitely determined. It should be borne in mind that there is a physiological alimentary glycosuria, caused by the ingestion of excessive amounts of any sugar, which has no pathological significance whatsoever.

The existence of many forms of transient non-diabetic glycosuria has led us in the past to underestimate, perhaps, the possibly serious import of an intermittently appearing spontaneous glycosuria, but of late we have been inclined to give a grave prognosis in these cases. Von Noorden[1] has recently expressed the following opinion: "When a transitory glycosuria is accidentally discovered in an individual, the reason for which does not obviously lie in a diet excessively rich in sugar, I should like to recommend urgently that such an event be neither heeded lightly nor neglected. It is in most cases the warning signal of later diabetic disease, the outbreak of which may not occur for many months or even years." No definite statistics are quoted in support of this view.

We have been able to find in the literature but 9 cases of transitory or spontaneous glycosuria which were followed until they developed diabetes. These cases are reported by Raphael,[2] Kraus and Ludwig,[3] H. Straus,[4] Bierens de Haan,[5] and Van Oordt;[6] Cantani[7] also speaks of such cases, but gives no figures. The time elapsing between the first observed glycosuria and the development of diabetes in all cases was one year or less, with the exception of von Norden's case of diabetogenous obesity, in which the time was four years.[8]

Answers to the questions, (*a*) How many of the cases of spontaneous glycosuria develop later into diabetes? and (*b*) Is there any way of identifying these cases at an early date? would add to our knowledge of this disease, enable us to give a more intelligent prognosis in these very perplexing cases, and possibly spare some patients a most irksome treatment.

[1] Disorders of Metabolism and Nutrition: Diabetes. English trans., 1905, p. 147.
[2] Ztschr. f. klin. Med., xxxvii, p. 20.
[3] Wien. klin. Woch., 1891, p. 855-897.
[4] Deut. med. Woch., 1897, Nos. 18 and 20.
[5] Archiv f. Verdauungsk., Band iv, Heft 1, p. 4.
[6] Munch. med. Woch., 1898, No. 1.
[7] Der Diabetes Mellitus, 1877, German trans., 1880, p. 305.
[8] Verhandlungen des XIII Congress f. innere Medizin, 1895, p. 140.

Name.	Age	Sugar history.	Date of last normal urine examination.	Subsequent history.	Urine examination.	Fehling's.	Phenyl hydrazin.	Polariscope.	Fermentation.	Rotation after fermentation.	Remarks.
D. W.	31	Trace, 1900.	None made.	Healthy, gained 28 pounds.	24 hour spec., 1200 c.c., s. g. 1025. 2 hour post-glucose. 3 hour post-glucose.	—	—	per ct. — 0.15	—	.....	Free from diabetes, 1906.
A. A. C.	21	0.42 per cent., 1901.	None made.	Healthy.	Before and after lunch spec. 2 hour post glucose spec. 3 hour post-glucose spec	— +	+ —	— 0 3 — 0.2 — 0.225	— —	.....	Free from diabetes, 1906.
D. Y. W.	11	0.83 per cent., 1901.	1898 (Ins. Co.).	May, 1906, trace albumin, no sugar, hyaline and gran casts 1901 (6 weeks later), 0.48 per cent. glucose. Accepted by two Ins. Cos. Healthy.	24 hour spec., 817 c c., s. g. 1026. 2 hour post-glucose. 3 hour post-glucose.	— —	— —	0.0 0 0	... ...	— 0.2 per cent.	Free from diabetes, 1906.
H. M.	53	0.83 per cent., 1901. Trace of albumin; hyaline casts.	None made.	Lost 40 pounds. 1901, chronic nephritis and uremia. 1905, the same. 1906, chronic nephritis.	24 hour spec., 1400 c.c., s. g. 1020.	—	—	0.0	...	.....	Free from diabetes, 1906.
J. N.	57	0.37 per cent., 1901.	None made.	April, 1901, no glucose, accepted by three companies since. Healthy.	13 hour spec., 915 c.c., s. g. 1022.	—	—	0.0	...	.....	Free from diabetes, 1906.
P. E. G.	36	Trace, 1895. 0.83 per cent., 1901 (0.25 per cent. next day).	None made.	Healthy, urine frequently negative for sugar.	24 hour spec., 1500 c.c., s. g. 1018. 2 hour post-glucose. 3 hour post-glucose.	— —	— —	0.0 — 0.25 — 0.5	...	.....	Free from diabetes, 1906.
A. B. H.	43	Small quantity, 1900.	None made.	Healthy, urine negative once.	24 hour spec., 1550 c.c., s. g. 1015. 2 hour post-glucose. 3 hour post-glucose.	— —	— —	0.0 — 0 05 — 0.1	— ...	.....	Free from diabetes, 1906.
A. S. S.	39	0.67 per cent., 1901.	1898.	Healthy, 2 urinalyses since negative.	12 hour spec., 850 c.c., s. g. 1027. 2 hour post-glucose. 3 hour post-glucose.	— —	— —	0.0 0.0 0.0	— —	.....	Free from diabetes, 1906.
I. A. B.	31	0.83 per cent., 1900 (found twice).	None made.	Has lost 30 pounds, extremely neurotic. Urine frequently negative. Nov., 1902, 0.66 per cent. glucose (Ins. Co.). 1903, cane-sugar test neg. (Ins. Co.).	24 hour spec., 730 c.c., s. g. 1025. 2 hour post-glucose. 3 hour post-glucose.	— —	— —	— — 0.1 — 0.2	— ...	.....	Free from diabetes, 1906.

	51	0.42 per cent., 1900.	None made.	Healthy, urine frequently negative for glucose (physician).	24 hour spec., 1100 c.c., s. g. 1026. 2 hour post-glucose. 3 hour post-glucose.	— + —	— + +	— 0.5 — 0.25	... ...	....	Free from diabetes, 1906.
A.	27	0.42 per cent., 1901.	1893 (Ins. Co.).	Accepted twice by Ins. Co. 2 attacks pneumonia. July, 1903, after 100 gm. cane sugar, 0.67 per cent. glucose (trace glucose 1903, after sugar meal).	24 hour spec., 860 c.c., s. g. 1020. 2 hour post-glucose. 3 hour post-glucose.	— — —	— — —	0.0	—	....	Free from diabetes, 1906.
	32	Trace, 1895, 1.1 per cent., 1901.	1890 (Ins. Co.).	1903, trace sugar (Ins. Co.). Healthy, urine frequently negative.	24 hour spec., 1020 c.c., s. g. 1030. 2 hour post-glucose. 3 hour post-glucose.	— + —	— + —	0.0 + 0.3 — 0.125	... + —	....	Family history, diabetes; very suspicious case.
	33	0.56 per cent., 1901, none next day.	None made.	Accepted by 2 companies. Jan., 1902, 3.3 per cent. sugar Jan., 1904, 1.1 per cent. sugar. Healthy.	24 hour spec., 1010 c.c., s. g. 1022. 2 hour post-glucose. 3 hour post-glucose.	— + —	— + —	0.0 + 0.3 — 0.125	+ —	.....	Very suspicious case.
	41	Small quantity, 1901.	None made.	Healthy, urine frequently negative for glucose. Dec., 1902, 0.56 per cent. Dec., 1903, after 100 gm. sugar 1.2 per cent. glucose.	12 hour spec., 780 c.c., s. g. 1026. 12 hour spec., 265 c.c., s. g. 1024. 2 hour post-glucose. 3 hour post glucose.	— — + —	— — + —	0.0 0 0 + 0.1 — 0.1	— — —	....	Suspicious case.
	43	0.67 per cent., 1900.	None made.	Healthy.	12 hour spec., 635 c.c., s. g. 1022. 2 hour post-glucose. 3 hour post glucose.	— + —	— + ...	0.0 + 0.1	+ ...	....	Very suspicious case.
	31	Trace, 1898. Trace, 1899.	None made.	Urine frequently negative for glucose. Developed tabes. 1904, after 100 gm. cane sugar 0.42 per cent. glucose.	24 hour spec., 885 c.c., s. g. 1024. 2 hour post-glucose. 3 hour post-glucose.	— + +	— + +	0 0 + 0 4 + 0.1	+ +	— — 0.2 per cent.	Suspicious case.
	38	Trace, 1898. 0.56 per cent., 1900.	None made.	Healthy. June, 1904, 0.67 per cent., frequently traces found by physician, frequently absent.	24 hour spec., 1450 c.c., s. g. 1026. Before glucose. 2 hour post-glucose. 3 hour post-glucose.	— + + —	— + + +	0.0 + 0.3 + 2.5 — 0.4	... + + —	..... — 0.5 per cent. - 0.1 per cent. — 0 35 per cent.	July, 1906, one hour after lunch specimen showed 0.8 per cent glucose. Diabetes.
	36	Trace, 1899. Trace, 1900.	1899, normal.	Healthy. Sugar frequently found in traces since, frequently absent.	24 hour spec., 1010 c.c., s. g. 1033. Before glucose 2 hour post-glucose. 3 hour post-glucose.	+ + + —	+ + + +	+ 0.1 + 0.05 + 2 7 — 0 2	... + + —	..... — 0.1 per cent., no ozanon. —0.225 percent	Family history, diabetes. Diabetes.
	34	Trace, 1900.	1890-98 normal 4 times, 1898.	Healthy. Sugar frequently found in traces, frequently absent.	9 hour spec., 935 c.c., s. g. 1026. Before glucose. 2 hour post-glucose. 3 hour post-glucose.	+ + + +	+ + + +	+ 0.8 0 0 + 3 5	+ + +	— 0.12 per cent., no ozanon.	Diabetes.
	18	0.33 per cent., 1901; 2 days later, 0.37 per cent.	1891.	Healthy. Sugar occasionally present or absent.	24 hour spec., 2000 c.c., s. g. 1028. Before glucose. 2 hour post-glucose. 3 hour post-glucose.	+ + + +	+ + + +	+ 0 3 + 0 1 + 1.6 + 1 6	+ + +	— — 0.15 per cent — — 0.18 per cent.	Diabetes.

With these particular ends in view we have undertaken this research, and we have been given an opportunity for the partial elucidation of the questions at issue in the extensive material very courteously placed at our disposal by the medical directors of one of New York's large insurance companies.

We selected from the company's records all of the New York City cases showing a glycosuria of 1 per cent. or less during the years 1900 and 1901, choosing these slight glycosurias so as to exclude, if possible, all diabetics. This gave us 69 cases, of which 24 could not be traced. Of the 45 left, 20 joined cheerfully in our research, while 25 refused to do so. However, we did ascertain that these diffident 25 were alive, and at least 13 of them, whom we interviewed personally, were apparently in good health.

The preceding table summarizes the histories of the 20 cases which form the basis of our work, and the results of our examinations and experiments carried out on them during the summer of 1906.

In regard to their previous history we see that 8 subjects had shown normal urine on examination either by an insurance company or their own physician at periods varying from three weeks to ten years before sugar was first discovered. Twelve subjects had never had their urine examined before. We have records of sugar having been found once in three men and twice in two men prior to 1900. Of the 15 remaining cases, with their first record of sugar in 1900 and 1901, 7 showed it again at some subsequent period; 17 of the 20 subjects showed normal urine (office specimens) at least once after the sugar was first discovered. Some of them, it is true, observed spasmodically a restricted diet. The remaining 3 gave normal twenty-four-hour specimens in 1906.

We may, therefore, group all of these cases together as cases in which a transient spontaneous glycosuria was first discovered some time between 1895 and 1901, and in no case could we then say that anything more than a transient spontaneous glycosuria existed. Of course, we do not know the exact date at which the glycosuria was first present, nor can we say positively that the initial glycosurias were not the result of a diet excessively rich in sugar, although as far as the memories of the subjects served, this particular supposition was negatived by our 20 cases.

There is no doubt that these men showed glucose in their urine in 1900 or 1901. A specimen of urine was passed in the presence of the insurance physician and was examined by him with Fehling's solution. If it reduced Fehling's it was sent to an experienced chemist, who re-tested it with Fehling's solution, with phenyl hydrazin, by fermentation, and with the polariscope.

We obtained twenty-four-hour specimens from 14 men, twelve-hour specimens from 5, and small, before and after lunch, specimens from 1. We found all but 2 of the subjects in excellent health, 1 suffering from chronic nephritis and 1 from tabes; 9 had

gained in weight, 9 had remained stationary, and 2 had lost weight. No evidences of arteriosclerosis could be detected except in the case of nephritis, and aside from the urine there was nothing to suggest diabetes in any of them. In the group of 5 cases showing sugar previous to 1901, 2 had developed a constant slight spontaneous glycosuria (one of them having a family history of diabetes) and could be called diabetic, although the glycosuria was the only symptom present. Of the 15 remaining subjects who had first shown sugar during 1900 and 1901, 2 had developed a constant slight glycosuria, but showed no other diabetic symptoms.

Thus 4 of the 20 subjects developed mild diabetes in from five to eight years. The 16 remaining showed normal twenty-four-hour specimens. At a later period 18 of these men were each given 100 grams of glucose during the forenoon, about three hours after breakfast. We then secured from them specimens of urine passed two and three hours after the ingestion of glucose. No food was taken during this time. Our results are also included in the foregoing table.

The interpretation of these results introduces the subject of the relation between transient spontaneous glycosuria and glycosuria *e saccharo*.

THE RELATION BETWEEN TRANSIENT SPONTANEOUS GLYCOSURIA AND GLYCOSURIA E SACCHARO.

By this we mean the relation existing between the ordinary spontaneous glycosuria, as exemplified in the 20 cases just considered, and the glycosuria produced in cases of this kind by the ingestion of 100 grams of glucose or saccharose. We hope to show that we have in this estimation of the sugar tolerance a means of determining at a relatively early date which cases of spontaneous glycosuria will become diabetic.

Some technical terms and the details of experiments with alimentary glycosuria must now be considered. By the assimilation limit for any sugar, a term first used by Hofmeister,[9] we mean that quantity of sugar necessary to be ingested in order to produce a trace of sugar in the urine. Individual susceptibility is an important factor in fixing this assimilation limit, for the same quantity of sugar will not produce glycosuria in all healthy people, even if given proportionately to the body weight (Moritz).[10] There also are transitory conditions, entirely physiological, which lower this limit (H. Strauss).[11] The assimilation limit for glucose varies from 150 to 200 grams (von Noorden).[12]

[9] Archiv f. experimentelle Pathologie and Pharmakologie, 1889, xxv, 249.
[10] Verhandl. X Congress f. innere Medizin, p. 125. [11] Deut. med. Woch., loc. cit.
[12] Disorders of Metabolism and Nutrition: Diabetes. Eng. trans., 1905, p. 33.

Whether the sugar is given on an empty stomach or not has a bearing on the result. Glucose is carried from the intestine by the portal vein and deposited in the liver as glycogen. If the intestine is suddenly overloaded with glucose a very small portion may be absorbed by the thoracic duct (von Noorden)[13] and excreted by the kidneys, without going through the liver. Thus a slight glycosuria, occurring after glucose taken on an empty stomach, does not necessarily mean that there is a superabundance of glycogen in the liver.

If it takes 150 to 200 grams of glucose to produce glycosuria in a normal man, production of glycosuria by 100 grams would prove conclusively that the assimilation limit for glucose was lowered at that particular time. H. Strauss[14] carried out experiments on 50 subjects, giving each 100 grams of anhydrous glucose dissolved in 500 c.c. of water, on an empty stomach, and produced slight glycosuria in but 4. On repetition of the experiment, however, these 4 were negative.

The assimilation limit for cane sugar is the same as that for glucose, 150 to 200 grams (von Noorden).[15] Sometimes, owing to changes in the intestinal ferments, cane sugar, or saccharose, fails to split up and is excreted as cane sugar, the liver being unable to appropriate it in this form. However, if glucose is excreted after the ingestion of 100 grams of cane sugar, we can infer that there is an excess of glycogen in the liver; so, whether we conduct our experiments with cane sugar or glucose, the results are the same, provided we test always for glucose.

The results of experiments with cane sugar on healthy people are somewhat contradictory. Linossier and Roque[16] found glucose in the urine in 5 cases after the ingestion of from 50 to 100 grams of cane sugar on an empty stomach. Worm-Müller[17] found in 1 case glucose in the urine after the ingestion of 50 grams of cane sugar. Moritz[18] states that he always found glucose in the urine after large quantities of cane sugar had been taken.

There are few recorded experiments with cane sugar on normal people, using the standard dose of 100 grams, and not giving it on an empty stomach, so that it seemed advisable to carry out an experiment under proper conditions. Ten of the third-year students of the Cornell University Medical College kindly volunteered for the experiment. Each showed a normal twenty-four-hour specimen and a normal specimen just before taking the cane sugar. At 10 A.M. 100 grams of chemically pure cane sugar dissolved in 350 c.c. of water was administered to each of them.

[13] Handbuch. der Pathologie des Stoffwechsels, von Noorden, p. 29.
[14] Deut. med. Woch., loc. cit.
[15] Disorders of Metabolism and Nutrition: Diabetes. Eng. trans., 1905, p. 34.
[16] Arch. de méd. exper., 1895, vii, p. 228.
[17] Pflüger's Archiv f. Physiologie, 1884, Band xxxiv, p. 576.
[18] Loc. cit.

Specimens were taken one, two, three, and four hours afterward, no food being taken in the interim. The following table shows the results:

October 30, 1906.		Fehling's solution.	Polariscope.	Ozanon.	Fermentation.	Rotation after fermentation.	Remarks.
			per cent.			per cent.	
W.	10.00 A.M.	—					
	11.00 "	—	— 0.3	—			
	12.00 M.	—	— 0.2	—			
	1.00 P.M.	—	— 0.1	—	—		
	2.00 "	—	— 0.1	—	—		
S.	10.00 A.M.	—	— 0.1				
	11.00 "	—	— 0.2	—	—		
	12.00 M.	—	— 0.225	—			
	1.00 P.M.	—	— 0 1	—			
	2 00 "	—	— 0.1	—			
S.	10.00 A.M.	—	— 0.3	—	—		
	11.00 "	—	— 0.3	—			
	12.00 M.	—	— 0.3	—	—		
	1.00 P.M.	—	— 0.3	—			
	2.00 "	—	— 0.1	—			
F.	10.00 A.M.	—	0.0				
	11.15 "	—	— 0 1	+	+	— 0.18	No invert sugar.
	12.10 P.M.	—					
	1 00 "	—	— 0.1	—	—		
	2.00 "	—	— 0.1	—	—		
O. B.	10.00 A.M.	—	0.0				
	11.00 "	+					
	12.00 M.	+	— 0 5	+	+	— 0.4	
	1.00 P.M.	—	— 0 1	—	—	.....	Gave Sellwanoff's reaction for levulose.
	2·00 "	—	— 0.1	—	—		
C.	10.00 A.M.	—	— 0.1				
	11.15 "	—	— 0.3	—	—		
	12.30 "	—	— 0 3	—	—		
	2 00 P.M.	—	— 0.2	—			
	3.00 "	—	— 0.2	—			
B.	10 00 A.M.	—	— 0 3				
	11.00 "	—	— 0.2	+	+	— 0.25	
	12 00 M.	—	— 0.2	+			
	1.00 P.M.	—	.....	—			
	2.00 "	—	— 0.15	—			
K.	10.00 A.M.	—	— 0.15				
	11.00 "	—	— 0.2	—			
	12.00 M.	—					
	1.00 P.M.	—	— 0.2	.....	.....	.....	No invert sugar.
	2.00 "	—	— 0.1				
Z.	10.00 A.M.	—	— 0.05	—			
	11.10 "	—		—			
	12.10 P.M.	—	— 0 25	+	+	— 0 3	
	1 15 "	—		+			
	2.00 "	—	0.225	—			
B.	10 00 A.M.	—	0.0				
	11.00 "	—	0 0		+		
	12 00 M.	—	— 0.15	—	—		
	1.00 P.M.	—	— 0 1	—	—		
	2.00 P.M.	—	— 0.15	—	—		

We found that 3 cases showed about 0.05 per cent. of glucose, and 2 gave traces of glucose. These quantities of glucose are so small

that they are negligible. Nine showed an increase in the levorotatory substances, the percentage varying from 0.2 to 0.4. The Kowarsky modification of the phenyl-hydrazin test was used, and the precipitate examined at the end of one hour. The percentage of glucose was estimated by the Schmidt and Hansch polarizing saccharimeter.

We see, therefore, from H. Strauss' experiments on 50 normal people with glucose, and from our experiments on 10 normal people with cane sugar, that the ingestion of 100 grams of either substance will not produce more than mere traces of glucose in the urine of healthy individuals.

A large amount of work has been done with alimentary glycosuria, both *e saccharo* and *ex amylo*, its object being a more exact knowledge of the nature of diabetic glycosuria, but the results have been rather contradictory. The only reference von Noorden makes to these investigations, as far as we can find, is in his *Lectures on Diabetes*,[19] where he says: "They (the experiments with alimentary glycosuria) did not fulfil this expectation, but brought to light many points of interest." Naunyn[20] says that an alimentary glycosuria *e saccharo* may be a diabetic glycosuria, but not necessarily, and most frequently is not. If we find it present after 100 grams of glucose, a suspicion of diabetes exists. If the sugar exceeds 1 per cent., the suspicion is very urgent. Raphael,[21] as a result of his experiments, is constrained to think that these two forms (alimentary *e saccharo* and diabetic glycosuria) have no important difference. J. Strauss[22] says: "From all this I am obliged to conclude that the alimentary glycosuria *e saccharo* is also to be placed in the category of diabetic disturbances of metabolism." H. Strauss,[23] who worked chiefly with alcoholics and the traumatic and non-traumatic neuroses, concluded that in the majority of the conditions in which an alimentary glycosuria is noted a transient glycosuria is also frequently observed, and the glycosurias generally disappear at the same time.

One reason, perhaps, for these diverse opinions is that many of the experiments have been carried out in pathological conditions of the body, such as chronic alcoholism, paralysis, meningitis, etc., which have but a slight and limited relation to diabetes. The ordinary transient spontaneous glycosuria, however, presumably the earliest manifestation of diabetes and a most promising field for experimentation, has been comparatively neglected, probably owing to the scarcity of available material.

We have found only 7 cases of spontaneous glycosuria in the literature, in which the reaction to glucose or cane-sugar ingestion was ascertained. F. Raphael[24] reports 2 cases which show alimentary

[19] English trans., 1905, p. 38.
[20] Nothnagel's Specielle Pathologie und Therapie der Diabetes Mellitus, p. 19.
[21] Ztschr. f. klin. Med., xxxvii, p. 48.
[22] Ibid., xxxix, p. 292.
[23] Deut. med. Woch. Loc. cit.
[24] Ztschr. f. klin. Med. Loc. cit.

glycosuria ranging from 1 per cent. to 3 per cent., and in from one to two years developed diabetes. Von Noorden[25] reports 1 case showing 1 per cent. of alimentary glycosuria, which developed in one month a constant glycosuria. B. de Harn[26] also reports 1 case which gave an alimentary glycosuria of 0.9 per cent. and in less than a year developed diabetes. J. Strauss[27] reports 3 cases, previously showing an alimentary glycosuria, but gives no percentages nor the subsequent history of his cases.

All of the above cases of spontaneous glycosuria, excepting the 3 of J. Strauss, showed a marked alimentary glycosuria and developed diabetes in a short time. The experimental technique in these cases, however, varied widely, and, therefore, no basis is afforded for comparison with our results.

We shall now consider the results of our experiments with the production of alimentary glycosuria, in our 18 cases of transient spontaneous glycosuria. These were conducted, as explained in the previous section, under similar conditions, during the summer of of 1906. (See first table.)

Four showed an alimentary glycosuria of from 1 per cent. to 3 per cent., these being the 4 diabetics, additional evidence of the correctness of our diagnosis; 5 showed from 0.1 per cent. to 0.4 per cent. of glucose, and 2 showed only traces of glucose, not sufficient being present to estimate quantitatively; 7 were negative. Of the 5 showing measurable quantities of glucose, cases C. K., M. G., and E. S. we strongly suspect are diabetic at the present time, because of their past history and their decided reaction to the test. In view of our experiments with cane sugar on the 10 students, and H. Strauss' experiments with glucose on 50 normal people, we attach no importance to the results on the test of those 2 cases which reacted only to the phenylhydrazin test.

If we regard alimentary glycosuria *e saccharo* as a disturbance of metabolism essentially diabetic in nature, we may, in the light of this test, again summarize our results as to the subsequent history of 18 subjects of transient spontaneous glycosuria, and say that 4 have become diabetic, 3 are probably diabetic, and 2 are suspicious cases, while 9 are not diabetic; 1 of the 2 who refused the test is a chronic nephritic, and the other never showed sugar after 1901, although examined repeatedly, and gave a normal thirteen-hour specimen. So there is little doubt that these 2 also are free from diabetes. This makes 11 altogether free. These results, 4 diabetics and 5 probable diabetics out of 20 cases, contrast decidedly with our previous results stated at the end of the first section, when we found that but 4 had become diabetic and 16 were presumably healthy.

It will be remembered that 18 of our subjects were examined

[25] Verhandlungen der XIII Congress f. innere Medizin, 1895, p. 180.
[26] Archiv f. Verdauungskrankheiten. Loc cit.
[27] Ztschr. f. klin. Med., xxxix, p. 202.

again some time after sugar had first been found, and 11 of them showed a glycosuria on this second examination. These 11 included the 4 diabetics, 4 of the suspicious cases, and 3 cases now normal. This exemplifies the prognostic value of a repeated detection of traces of sugar.

We also found that 5 of these 20 cases, in addition to glucose, excreted a levorotatory substance varying from 0.2 per cent. to 0.4 per cent. (as estimated by the saccharimeter), which substance did not ferment, gave a positive reaction to Bial's test and the phloroglucin test, and with the spectroscope showed a broad band between C and D. It seems fair to assume that this was combined glycuronic acid. Three of the cases showed no glucose, but did show from 0.2 per cent. to 0.5 per cent. of this same substance. It will be noted that the sugar excretion reached its maximum in the two-hour post-glucose specimens.

The insurance company carried out experiments in alimentary glycosuria during 1903 and 1904 on all sugar cases, and it will perhaps be of some help if we compare their results in the spontaneous glycosurics with our results.

THE INSURANCE COMPANY'S EXPERIMENTS. Tests were made by the company over a period of eighteen months. All applicants having a history of sugar were given, in a small number of cases, 100 grams of glucose, in the greater number, however, 100 grams of cane sugar, dissolved in 300 c.c. of carbonated water, at some time in the forenoon or afternoon. Then a specimen of urine was obtained approximately three hours after, but this time varied considerably. No restrictions as to eating during the interim were made. As explained above, there is no difference in the results of the glucose or cane-sugar test, provided we consider it positive only in the presence of glucose in the urine.

Obviously, tests which were conducted under such varying conditions possess much less value than ours, and deductions therefrom are correspondingly limited. We selected from the records all cases showing a spontaneous glycosuria of less than 1 per cent. to which the test was applied within one year of the discovery of sugar. These were men who presented no symptoms of diabetes and believed themselves in excellent health at the time of the initial glycosuria. These formed a group of 19 cases of ordinary spontaneous glycosuria similar to our 18 cases, except that our cases did not receive the glucose test until at least five years had elapsed. The following table summarizes the company's results:

Name.	Date initial glycosuria.	Quantity of sugar.	Time elapsing between initial glycosuria and test.	Urine before glucose.	Urine after glucose.
		per cent.			
M. W. Z.	April 21, '01	0.48	4 months.	1024, no sugar.	1021 —0.48 per cent.
R. L.	April 4, '03 April 7, '03	0.83 0.56	3 months.	1024 "	1004 —0 56 "
S. B.	Jan. 3, '05	0 57	23 days.	1023 "	1022 —0.25 "
G. S. A.	June 14, '04	Trace.	8 months.	1026 "	1028 —0.5 "
T. B. B.	Nov. 25, '04	Trace.	3 months.	1016 "	1020 —0.44 "
A. A. K.	Jan. 17, '05	0.28	2 months.	1025 "	1030 —0.25 "
M. J.	June 20, '04	0.18	2 days	1020 "	1020, negative.
H. A.	Dec. 10, '04 Jan. 19, '05	0.22 0.33	1 day.	1025 "	1022 "
G. H.	Aug. 5, '04 Aug. 6, '04	Trace. Trace.	3 months.	1025 "	1025 —0.33 per cent.
B. E.	Jan. 18, '05	0.31	12 days.	1012 "	1006, negative.
C. B. A.	Jan. 15, '05	0 25	16 days.	1023 "	1018 "
E. M.	Nov. 3, '04	0 25	24 days.	1022 "	1021 "
H. H.	June 25, '03 Nov. 21, '04	0 42 0.67	10 days.	1020 "	1020 "
E. M. G.	July 11, '04	0 33	1 day.	1018 "	1022 "
J. M.	Dec. 30, '04	0 33	2 days.	1008 "	1020 "
A. S.	Nov. 14, '05	0.35	11 days.	1020 "	1020 "
J. T. H.	Feb. 3, '05	0 44	2 months	1016 "	1032 "
A. K.	Jan. 26, '05 Jan. 21, '05	0.24	14 days. 2 days.	1020 "	1020 "

Thus we see that 7 cases showed an alimentary glycosuria ranging from 0.2 per cent. to 0.6 per cent., and 12 were negative. It is interesting to note that these 7 positive cases received their glucose or saccharose test from three weeks to eight months after sugar was first discovered, while all of the 12 negative cases except 2 received their tests a few days after the discovery of sugar.

The only legitimate deduction to be made from these experiments is that at least 37 per cent. of a group of spontaneous glycosurics showed an alimentary glycosuria *e saccharo* within one year of the initial discovery of sugar.

As regards the time element in alimentary glycosuria we may here mention that F. Raphael[28] concluded, as a result of his experiments with the glucose test on susceptible patients (including his 2 cases of spontaneous glycosuria), that the sugar excretion varies in quite wide limits at different times, or may entirely disappear. These conclusions are supported also by the work of H. Strauss,[29] Arndt,[30] Rosenberg,[31] and Marin,[32] with the same tests in various diseased conditions.

Now, we found that 9 of our 18 cases showed a measurable alimentary glycosuria at the end of from five to eleven years, and the insurance company found that 7 of their 19 cases showed alimentary glycosuria at some time within one year of the first discovery of sugar. The obvious question is, Would the same cases showing alimentary glycosuria *e saccharo* within one year of the initial

[28] Ztschr. f. klin. Med. Loc. cit.
[29] Deut. med. Woch. Loc. cit.
[30] Deut. Ztschr. f. Nervenheilk., 1897, x, p. 419.
[31] Inaug. Dissertation, 1897: Alimentary Glycosuria, etc.
[32] Berl. klin. Woch., 1897, Nr. 52.

glycosuria also show it at the end of five years? In other words, do we possess in this test a means of deciding, at an early date, which cases of spontaneous glycosuria will show a continued disturbance in their sugar metabolism and ultimately develop diabetes?

Before answering this, let us sum up the data we have at hand:

1. Fifty per cent. of a group of spontaneous glycosurics showed alimentary glycosuria *e saccharo* at the end of five years, and included all of the diabetics and probable diabetics.

2. Of our 17 cases of spontaneous glycosuria reëxamined at some time between 1895 and 1906, 58 per cent. showed sugar again, 8 of these developing diabetes or probable diabetes.

3. In 2 of our cases, E. S. and W. E., we are able to trace the different phases of disturbed sugar metabolism from the first appearance of sugar to the development, years later, of possible diabetes. Thus spontaneous glycosuria in 1898 and 1901, again in 1899 and 1902, alimentary glycosuria *e saccharo* in 1903 and 1904, and again in 1906.

4. We know, from the insurance company's experiments, that at least 37 per cent. of a group of spontaneous glycosurics showed alimentary glycosuria *e saccharo* within one year of the initial discovery of sugar.

In other words, 50 per cent. of a group of spontaneous glycosurics showed a disturbed sugar metabolism (reaction to glucose) five years after the first discovery of sugar; 58 per cent. of the same group showed a disturbed sugar metabolism (reappearance of sugar in the urine) two or three years after sugar was first discovered. 37 per cent. of another group of spontaneous glycosurics showed a disturbed sugar metabolism (reaction to glucose) within one year of the first discovery of sugar. Finally, we can, in 2 cases, trace the disturbed sugar metabolism through the entire five years.

These various facts may be explained by an assumption which readily suggests itself, that is, the division, broadly, of spontaneous glycosuria into two types: (1) A class essentially diabetic from the outset, in which sugar recurs, which shows constantly glycosuria *e saccharo*, and which at the end of five or more years has become diabetic or probably diabetic. (2) A class, quite harmless, in which sugar does not recur after the first weeks and which does not show a glycosuria *e saccharo* except perhaps during the first few weeks, and does not develop diabetes. The glucose test, therefore, would seem to give important help in differentiating these two provisional types of spontaneous glycosuria at a relatively early date.

SUMMARY. 1. At the end of five years 20 per cent. of a group of spontaneous glycosurics had become diabetic, 15 per cent. had become suspicious cases, and 10 per cent. somewhat suspicious; 55 per cent. had remained free from diabetes.

2. Eight of eleven cases of spontaneous glycosuria, in which sugar recurred, became diabetic or probably diabetic.

3. The alimentary glycosuria arising from glucose or cane sugar, provided the test is properly conducted and repeated at intervals, affords a valuable aid to prognosis in cases of spontaneous glycosuria. A positive test is of much more value than a negative test.

4. Alimentary glycosuria *e saccharo* is essentially diabetic in its nature.

Von Noorden,[33] as a result of his belief that a transitory glycosuria "is in most cases the warning signal of later diabetic disease, the outbreak of which may not occur for many months or even years," advises in all of these cases "a moderate reduction of carbohydrate food and especially a complete exclusion of sweet comestibles." We found at the end of five years but 45 per cent., at the most, of our cases had become diabetic. If it is possible, as we believe, to detect these cases at a relatively early date, it would not seem necessary to maintain a permanently restricted diet in *all* cases.

If a small quantity of sugar is found in a patient's urine and there is no history of overindulgence in sweets, he should be placed on a restricted diet and his reaction to the glucose test ascertained frequently during the next six months. If the reactions are positive his restricted diet should be continued, even though the spontaneous glycosuria has not recurred. If the reactions are negative and sugar does not reappear, a restricted diet would seem superfluous.

The conflicting opinions as to the essential nature and diagnostic worth of alimentary glycosuria may be harmonized by more observations on the course of cases of spontaneous glycosuria, and by the frequent determination of their reaction to the glucose test.

We wish to express our thanks to Doctors T. W. Hastings and Mortimer Warren for several analyses.

INFANTILE SCURVY, ITS MANIFESTATIONS AND DIAGNOSIS.

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Infantile scurvy is a comparatively new disease, having been recognized for less than twenty years. The first edition of Osler's *Practice of Medicine*, which appeared in 1892, mentions the disease, but earlier text-books do not allude to it. In the periodicals devoted to pediatrics reports of cases of infantile scurvy began to appear about 1890. Even at the present time physicians do not always keep in mind that scurvy may occur in infancy, so that they often fail to recognize the disease. Because of the resemblance of some

[33] Disorders of Metabolism and Nutrition: Diabetes. English trans., 1905, p. 127.

of its symptoms to those of other diseases it may be of interest to consider its various manifestations and to emphasize its diagnostic features. Undoubtedly scurvy has occurred in infants for centuries, but it has not been sufficiently frequent for extended or careful study until the last two decades. During this period the very common use, by those who can afford it, of dried proprietary infant foods, or of sterilized milk, has greatly increased the number of such cases.

Formerly the condition was called acute rickets; but, strange to say, this form of rickets was almost always complicated by so-called "ulcerative stomatitis." Only last summer I heard of a typical case of infantile scurvy which was exhibited by a professor, at one of the great German schools of medicine, as a case of acute rickets with ulcerative stomatitis. So, even at the present day some of our German colleagues are barely aware of the existence of the disease in England and the United States: many of them claim that they do not have scurvy in Germany.

The French have become interested in looking for the disease, and for the last two or three years there have been frequent reports of isolated cases, occasionally of half a dozen cases; so they are finding it not a rare disease.

The English were the pioneers in the study of the disease and in the recognition of the distinctions between rickets and scurvy. Cheadle was of the opinion that "acute rickets," so called, was a compound of rickets and scurvy; Gee called the condition "osteal or periosteal cachexia;" while Barlow, after a study of eleven cases, with postmortem examinations of two, showed the essential nature of the disease and gave it the name "infantile scurvy." The Germans, with their tendency to fasten a proper name to every disease, call it Barlow's disease

Barlow summarized the chief features as follows: "(1) Predominance of lower-limb affection with (*a*) immobility, with the knee slightly flexed and thigh rotated outward, often pseudo-paralysis; (*b*) excessive tenderness; (*c*) general swelling of the lower limbs, due for the most part to subperiosteal hemorrhage; (*d*) skin shiny and tense, but seldom pitting and without undue local heat; (*e*) thickening of the shaft of the bone, made out when the swelling has disappeared; and (*f*) liability to fracture near the epiphysis. (2) Swelling of the gums, varying from definite sponginess down to minute transient ecchymoses. The conditions mentioned constitute the chief diagnostic criteria between scurvy and rickets in children. To these should be added (3) the tendency to hemorrhage either into the skin, subcutaneous tissues, mucous membranes, or rarely into the viscera, and (4) the definite and rapid improvement upon antiscorbutic diet."

Inasmuch as concrete instances are the best means of illustrating the disease, the following cases have been selected from among those I have seen in private practice to show both the more common,

as well as the unusual, phases of the malady. I have used only private and consultation cases for the reasons that their histories are more reliable and the patients were more carefully followed afterward than can be done in hospital and dispensary work.

CASE I.—*Pain, tenderness, and swelling in the lower extremities; blueness of the gums; pseudoparalysis of the legs. Developed while taking sterilized milk.*

Alice J., eight and one-half months old, was seen at Far Rockaway August 27, 1901, in consultation with Dr. Lewengood. The child had been fed from birth on modified milk made up and sterilized at the Walker-Gordon Laboratory. Barley-water had been used in the modification. Five weeks previous to the time I saw her, when just over seven months old, she began to have pain and tenderness in the legs, crying when the diaper was changed. Next she did not move the legs as usual, and later not at all; later still there was swelling of the lower part of the left thigh just above the knee. Three weeks previous to my visit a prominent orthopedic surgeon saw her and made the diagnosis of scurvy; he advised discontinuing the barley-water and substituting pasteurization of the milk for the sterilization; it was also advised that a splint be applied to the affected knee. For the week preceding my visit the baby had been getting worse, the milk meantime being both peptonized and pasteurized.

On physical examination I found the child ashy pale, with a dry, scaly skin; it did not cry, but lay motionless unless disturbed. There was intense tenderness in both lower extremities; so great was the fear of being touched that the child screamed out on the mere approach of her favorite nurse. A heavy tread near the bed would make her scream from the slight jarring. Both thighs were swollen, the left one being ten and one-half inches in circumference, the right nine and one-half inches. The bluish, tense, fusiform swelling of the left thigh was much like that of a rapidly growing sarcoma; but it was exquisitely tender, while the right thigh was less so. There was no crepitus to be felt in either thigh, that is, no sign of epiphyseal separation such as not infrequently occurs when the subperiosteal hemorrhage has existed for so long a time. The liver and spleen were markedly enlarged; there were no signs of rickets. There were no teeth, but the gums over the upper incisors were swollen and blue.

There was no question about the diagnosis, but only in regard to the treatment. Pasteurization of the milk, formula 3 per cent. fat, 6 per cent. sugar, and 1.5 per cent. proteids, was stopped, and orange-juice and beef-juice ordered to be given, a teaspoonful of each three times a day. In twenty-four hours the tenderness was less acute, and in a week the swelling was perceptibly smaller, the baby using her legs freely. Six weeks later there was still much enlargement of the left femur, a smooth exostosis remaining, comparable to the

result of cephalhematoma in the newborn. It was fully twelve months before the difference in the size of the two femora disappeared entirely.

Five weeks ago I saw the child. She is now six years old, weighs forty-six and three-quarters pounds, has perfect use of her legs, and is a splendid specimen of health. There are absolutely no evidences of her serious illness except a persistent slight enlargement of the spleen.

In this case the diagnosis was correctly made by the attending physician and the orthopedic consultant. A splint was applied, but the dietetic fault was not entirely eliminated.

CASE II.—*Tenderness of the thighs and ankles, swelling of the gums, and pseudoparalysis. Developed on pasteurized milk.*

James McC., eight and one-half months old, was first seen June 1, 1903. He had been a healthy child, fed from early infancy on modified milk from the Sheffield Farms laboratory. The laboratory directed the feeding, and changed the formula as necessary, I was told; moreover, I learned that the food had always been pasteurized. The formula being taken was: 4 per cent. fat, 5.6 per cent. sugar, 2.5 per cent. proteids, pasteurized.

For two weeks the baby had cried when the diaper was changed. The main complaint was that the baby was very fretful and did not use its legs naturally; the mother feared that the baby had paralysis. There was no digestive disturbance except constipation; no blood in the urine or in the stools.

Physical examination revealed a pale, flabby child covered with a purplish rash and clammy perspiration; there were no petechiæ. The gums about the four upper and two lower incisors were swollen and blue. The baby lay uncomplaining unless touched, but cried whenever the arms and legs were moved. He did not use the lower extremities at all, but moved the arms. There was great tenderness and some swelling of both thighs, the left thigh measuring seven inches, the right thigh measuring six. There was some tenderness and swelling above the ankles, and slight but distinct tenderness above the wrists. The heart was normal; there were a few coarse rales in the lungs; temperature 100.2° F., by rectum.

The pasteurization was discontinued, and the formula was 3.5 per cent. fat, 6 per cent. sugar, and 1.5 per cent. proteids ordered; also orange-juice, one-half ounce three times a day.

The next day it was reported that the baby was somewhat improved, being less fretful. The left thigh was one-quarter inch smaller and was less tender. On June 3 the left thigh was still smaller and the child brighter. On June 7 the child was playing with the left toe in his mouth. On June 8, one week after treatment was begun, the right thigh measured five and one-eighth inches, the left thigh six inches, a reduction of one inch in circumference during the week. Purée of potatoes was then added to the dietary.

Incidentally it was discovered that the baby was a masturbator by thigh rubbing. The mother averred that he would cry when caught doing this, and that he tried to conceal the act. Accordingly, a crutch was made to fasten to the thighs and keep them apart. Four weeks later the baby had gained three pounds.

It is to be noted that in this case the milk had simply been pasteurized, heated to 157° F. for twenty minutes, and no starchy food had been used.

CASE III.—*Tenderness; blood-blebs over the gums; pseudoparalysis. Developed while taking milk that was not heated when made, but overheated when warmed for the bottle feeding.*

Alice McS., twelve months old, was referred to me by Dr. M. C. O'Brien, on July 11, 1903. The child had been nursed for two months, then weaned because the breast milk failed; was given milk and barley-water for a while, then milk made up with peptogenic powder; then Mellin's Food; and then modified milk from the Walker-Gordon laboratory, formula 3.5 per cent. fat, 6 per cent. sugar, 1 per cent. proteid, made up with one ounce of dextrinized barley-jelly; next, the formula was changed to 4 per cent. fat, 6.5 per cent. sugar, 1.5 per cent. proteid with barley-water. The laboratory milk was neither sterilized nor pasteurized; but careful questioning elicited the information that the milk for several weeks had been heated in a saucepan to warm it before feeding. In this way it was probably heated to at least the temperature of pasteurizing, as a rule, and to a higher temperature often. The baby's digestion had improved, but there had been latterly some vomiting, so that the Walker-Gordon milk was stopped and a home-made formula used, as follows: 11 ounces of Borden's mixed milk, the whites of two eggs, 8 teaspoonfuls of Robinson's barley, boiled in sufficient water to make 40 ounces altogether.

The chief complaint was that the baby cried when the stockings were being put on or when the legs were moved; the mother thought that the baby had "paralysis partly." Moreover, the baby had a stool about every time it took food.

The child was very pale, an ashy pallor, and was covered with perspiration; it was merely fretful if let alone, but cried out when either the legs or arms were touched; there seemed to be tenderness of the spine and the baby would not sit up. The upper and lower gums bulged and were blue. There was little or no swelling to be found. There was a bruise-like discoloration on the dorsum of the right foot. Routine physical examination revealed signs of bronchitis in the chest.

The food was continued exactly as above save for the heating, which was discontinued; orange-juice and beef-juice were added. In one week the baby had improved so that it could be moved without crying; there was less tenderness of the legs and arms, so that the child began to move the legs and tried to sit up. The vomiting ceased and there were six to eight small normal stools per day.

Following this, the baby had bronchopneumonia and quotidian malaria. She recovered entirely from the scurvy symptoms in two weeks. I saw her in April, 1906, and operated on her for adenoids. She is now a fine rosy specimen of health, and shows not a trace of the disease.

CASE IV. *Bloody urine; tenderness of the extremities; bleeding from the bowels. Developed on pasteurized peptonized milk.*

Dorothea O., ten months old, was referred to me by Dr. L. Emmett Holt on July 21, 1909. The baby was not nursed at first, but was fed on sterilized modified milk, one-third milk and two-thirds water; then barley-water, then peptonized milk. She did not thrive, so that at two months she was given to a wet-nurse for three weeks. Becoming worse the nursing was discontinued and peptogenic milk pasteurized was again tried this time with fair success, as the baby gained so that the weight at seven months was 17½ pounds. At seven and one-half months blood was detected in the urine, which was being passed in very small quantity. There was no pain in the joints nor any change in the gums. The diet was changed and for three weeks the baby was given oatmeal gruel; during this time the urine became normal. When eight and one-half months old the peptogenic milk was made up with oatmeal gruel and pasteurized. At once blood and albumin reappeared in the urine, and this persisted. A simple modified milk was then tried and the stools became normal. Next the yellow, smooth, well-digested stools began to contain bright, sometimes frothy blood; the blood was both around and mixed in the stool. It had been noticed that, for three weeks before coming under my observation, handling the baby made it cry.

When examined July 24, 1909, the temperature was 101° F.; the respiration 34, the pulse 132, the weight 14 pounds. The baby was fairly nourished, but of ashy-gray color, due to an intense anemia with purplish mottling all over the body, giving a livid appearance; the skin was covered with clammy perspiration. The child's condition was very poor, bordering on collapse. The fontanelle was even with the general surface of the scalp, and one inch by one inch. There was one bluish spot one-quarter by one-half inch behind the right ear. Two lower central incisors had pierced the gum; around them the gums were dark purple and swollen. There were numerous fine, purple petechiæ on the chest, abdomen, and back. The child cried after moving the lower extremities; the arms were moved without pain. There was no swelling of the joints nor of the legs, but there was great tenderness just above both ankles, particularly the left, but no tenderness above the knees. The urine contained albumin and red blood cells, but no casts.

A diagnosis of scurvy was made, and so serious was the child's condition that it was feared she might die before the parents reached home.

The treatment instituted was to put the child on raw modified milk suitable for a three months' baby; to give also 1 ounce of orange-juice and one-half ounce of beef-juice, these to be doubled on the second day.

For two days the baby cried almost incessantly; on the third day the crying ceased and the legs could be moved without pain; and the blood disappeared from the urine and from the stools. On the sixth day the profuse sweating ceased and the gums returned to normal condition. Eight days after treatment was begun the baby had gained one pound in weight.

The first sign of scurvy in this case was the bloody urine; following this came tenderness of the legs and blood in the well-digested stools; next were seen the blood blebs around the teeth, and finally the petechiæ. The case emphasizes the marked tendency to hemorrhage from the mucous surfaces and into the skin which is produced by this nutritional vice.

CASE V.—*Blood in the stools and swollen; bluish gums. Developed on a weak milk mixture made up with starchy food.*

Ogden N., aged twelve and one-half months, was seen August 30, 1903. The patient had been under my care from the age of eight months. There was a marked rheumatic family history and a tendency to eczema; the child also had moderate adenoids not requiring removal. When nine months old the child contracted pertussis from his brother, and the whole family at once went to the country about May 15. At about the end of the whooping cough he developed a severe diarrhœa, on account of which the Walker-Gordon milk was stopped for a few days and broth given instead; then the milk was resumed in small quantity given with barley-water and alternated with broth. Every time the milk was increased to over one-fourth of the total food the stools became loose and filled with curds and mucus. On this account the milk was kept low, and for five weeks the child took 10 ounces of top milk (Walker-Gordon) raw, with 32 ounces of barley-water. A proprietary milk food (Nestlé's) was added to make up the deficiency in proteids. With care the milk was increased to 22 ounces of mixed milk, and the child did well for two weeks, when suddenly the stools became loose, at first only two movements in twenty-four hours, but both containing a little blood. On the following morning, August 31, the baby had six movements, all containing some flecks of blood. That afternoon I saw the child in the country and learned that there had been some loss of appetite and fretfulness for several days before the bowel trouble began. Naturally, I thought the case was merely a summer diarrhœa—an enterocolitis with a little blood. The temperature was only 100° F. by the rectum, and when the stools were shown they did not give evidence of intestinal indigestion, no curds, no mucus, no foul odor; moreover, the blood was not mixed with the stool nor with any mucus. The baby was very fretful and

further examination revealed nothing until I finally inspected the mouth. The gums were then seen to be much swollen and blue all around the four upper incisor teeth. There was no swelling nor tenderness at the extremities.

I stopped the barley-water and all starchy food at once, and ordered 2 ounces of orange-juice and 2 ounces of beef-juice; the food formula was made 2 ounces of mixed milk, raw, 2 ounces of lime-water, and 6 ounces of water. The next day the gums were better, being much less swollen; in two days the stools were free from blood and only two in twenty-four hours. The unboiled milk was rapidly increased and the child became speedily well.

In this case if there had not been any bulging and blueness of the gums I should have considered it ordinary enterocolitis. The rapid disappearance of the blebs of blood around the upper incisors when antiscorbutic measures were used, together with the subsidence of the diarrhœa and the disappearance of blood from the stools when the orange-juice and beef-juice—both well-known laxatives—were given, showed the case to be one of scurvy with hemorrhage from the intestinal mucous membrane.

CASE VI.—*The spinal joints remaining tender after the usual symptoms disappeared. Developed while taking milk and oatmeal gruel dextrinized by Cereo, a preparation of diastase.*

Van Wyck R., aged fourteen months, was first seen July 19, 1901. The family history was markedly rheumatic. The infant, healthy at birth, had been nursed entirely for two weeks; nursing was then supplemented by bottle food for a time and weaning was complete at six weeks. The successive foods taken by the baby were: (1) Mellin's Food with milk and water, the milk not being boiled; (2) malted milk, made up with boiled water; and (3) raw milk with barley-water dextrinized by Cereo. These various changes were made up at the end of the second month, when milk with oatmeal gruel and Cereo was begun. By the ninth month the proportions reached were about equal parts of oatmeal gruel and milk. After two and one-half months on this diet, when eleven and one-half months old, the baby stopped using his legs, and seemed to have pain when the legs were lifted to change the diaper. He kept his knees stiff. Next blue spots and some swelling appeared below the knees; but none over the knee-joint. There was also blue swelling of the gums and a bruise-like discoloration of the soles of the feet. When the child was at its worst, the gums would bleed. After about two weeks in this condition, because of almost complete loss of appetite, the mother changed the diet by adding beef-juice, soft-boiled egg, and mutton broth; orange-juice also was given occasionally. The main symptoms remaining when I first saw the child were inability, or rather refusal, to sit up and an ashy pallor.

On examining the baby, I found many evidences of rickets in the enlarged epiphyses at the wrist and the lateral furrows at the

lower part of the chest; there was also marked enlargement of the spleen and liver. The child used its legs quite well and the tenderness of the legs had disappeared. There remained, however, the discoloration of the skin on the shins and soles, due to subcutaneous hemorrhage. The most important symptom was crying when raised up to a sitting posture; the baby could not be persuaded to sit up. Careful examination revealed marked tenderness of all the spinal joints. There was no knuckle and only slight spasm of the spinal muscles upon lateral flexion. The gums showed blueness, softening, and bulging between the upper incisor teeth. The diagnosis was plainly scurvy and rickets.

A proper *régime* was established, and fresh food with raw milk and animal fats were given; the carbohydrate food was discontinued. Within a week the mother reported the greatest improvement in the baby's temper, comfort, and animal spirits. The child was not seen again for two months, inasmuch as he lived up the State. When seen the "bruises" had entirely disappeared; the child sat alone, would creep, stand, and push a chair about the room. All tenderness had disappeared from the joints of the spine.

The spinal tenderness in this case was quite marked. I had never read of nor seen such a condition in scurvy; but it seemed comparable to "typhoid spine." Dr. Henry Ling Taylor tells me he has seen this spinal tenderness in cases of scurvy, and that he reported such a case.[1]

CASE VII.—*Stiffness and swelling of one knee simulating arthritis. Developed while taking a proprietary food with heated milk.*

James S., Jr., aged nine months, was seen November 18, 1904. This child was also one of my own patients, so that the feeding history is accurately known. He had been perfectly healthy and digesting his food well until the hot spell in July, 1904. At that time, when five months old, he was taken acutely ill while in the country with vomiting and diarrhœa. The trained nurse, who had been with the child since birth, managed the case very well, and in a few days the child was taken to the seashore. At first the food was simply whey; then alternated with Nestlé's Food. From August 1 to October 15 the baby had an increasing quantity of fresh milk until he was taking equal parts of milk and water, with the addition of Nestlé's Food. The baby gained in weight from 14 pounds 11 ounces, the lowest weight, to 18½ pounds on September 30, 3½ pounds during the two months of August and September. On October 14, just two and one-half months from the time the milk and Nestlé's Food were begun, I received word from the nurse that the baby seemed to have colic at night; was very fretful, awaking about every hour. The family was in Tuxedo for the autumn, so I tried to advise by telephone. The baby's appetite was poor, and he had lost

[1] Archives of Pediatrics, September, 1894.

5 ounces during the week. Orange-juice and dilution of the food were ordered. On October 17, three days later, the report came that the baby was still having colic, though the stools seemed all right. The next day I saw the baby in Tuxedo, and found that the nurse had already observed the fact that the child did not care to lie down, and that he did not use his legs as much as usual. On examining the stools I found them normal; the abdomen revealed nothing; the heart and lungs were negative; there was no swelling or bleeding of the gums nor signs of teeth coming. The urine was normal. The temperature was 99.4° F. On examining the lower extremities, I found some swelling and tenderness of the right knee. Measurements showed the right knee 8½ inches, left knee 8 inches. The baby had lost 11 more ounces in two days, then weighing 17 pounds.

The probable diagnosis was clear, but the causative element seemed lacking. On careful questioning of the nurse I learned that the hot prepared proprietary food had always been added to the fresh milk without having been cooled. The previous food was stopped and formula of 3½ ounces of fresh mixed milk, 1 ounce of lime-water, 1 tablespoonful of milk sugar, and 3½ ounces of water was substituted. The orange-juice was increased to 4 ounces daily.

The next day the so-called colic was less and the baby began to move the leg; the swelling immediately began to subside, and was gone in three days more. In one week the baby had gained 3 ounces. On November 16, when the family returned to town, the left knee measured 7½ inches and the right knee 7¾ inches; there was absolutely no tenderness.

The prompt subsidence of the tenderness and swelling when the heating of the milk and the proprietary food were discontinued and the fruit-juice increased showed the case to be due to a dietetic error and the condition to be scurvy.

SYMPTOMATOLOGY. It will now be interesting to consider the results of the most important investigation of the disease yet made. This is the collective investigation of infantile scurvy by the American Pediatric Society. Next to Barlow's writings, this report is the most valuable contribution to this subject.

Statistics of 379 cases were collected, the reports coming from 138 physicians all over the United States and Canada. Summarizing the results, this investigation showed that the disease appears with equal frequency in male and female infants, for the most part between the age of seven and fourteen months. Nearly two-thirds of the cases appear during the latter half of the first year, and about two-fifths during the eighth and ninth and tenth months. The youngest patient was three weeks old, a breast-fed baby; the oldest patient was nine years of age. The cases reported were mostly from private practice with good hygienic surroundings.

One might almost say that the hygiene of the food, so far as sterilizing and great care against germs are concerned, is altogether too good. We rarely observe scurvy in tenement patients or those that are recklessly fed; since the taste of this bit of fruit or of potato or other table food prevents the development of scurvy that might occur from the use of patent foods or even boiled or sterilized milk, which is quite commonly used by the tenement-house population.

As regards causation, the investigation showed that the food seemed to be the most important etiological factor. Strange to say, in 10 cases the symptoms came on when breast milk had been the sole food from birth. The breast milk examined chemically from some of these cases proved to be totally inadequate for the needs of nutrition, and the infants were victims of mal-nutrition in these cases before the signs of scurvy appeared. But by far the greatest number of cases developed while the infants were being fed on some proprietary or starchy food, with or without milk, and on sterilized, pasteurized, or peptonized milk. The lack of freshness, or of fresh proteid particularly, seemed to be the main factor in each case in which the proprietary and starchy foods or the heated milk were used; in the breast-fed infants there seemed to be a deficiency of these vital proteids.

As to the manifestations of the disease, the symptoms first seen were, in order of frequency, pain and tenderness of the extremities, sponginess or puffiness of the gums, disability, anemia, cutaneous hemorrhages, swellings, and rarely hematemesis, hemorrhage from the rectum, and hematuria. Proptosis, protrusion of the eyeball, due to hemorrhage into the back of the orbit, and often hemorrhage under the conjunctiva, have been noted as the first symptom by English observers.

Dr. Richard Kalish, in a personal communication, speaks of 3 such cases he had seen; in 1 of these a corneal ulcer developed. Dr. Snow, of Buffalo, reported 1 such case at the 1905 meeting of the American Pediatric Society.

The pain and tenderness were usually noticed only on motion or handling; at times they may be so exquisite that the child screams when anyone approaches the bed or even looks at the child, for fear of being touched or jarred. The tenderness and swelling are found most frequently in the lower extremities, especially over the lower part of the femur or the lower part of the tibia. Very rarely the upper extremities alone, one or both, may be affected; generally the arms are involved after the thighs or legs. Fracture, really separation of the epiphysis, occurred only a few times.

The gums escaped in only 16 out of 379 cases. There were all degrees of involvement, and it must be borne in mind that the gums are frequently affected even when there are no teeth yet cut through. There were cutaneous hemorrhages in over 50 per cent. of the cases; bleeding from the mouth or gums in about 25 per cent., from the

nose in 9 per cent., from the bowels in 10 per cent., and hematuria in about 6 per cent. of the cases.

Symptoms of rickets were present in varying degrees in nearly one-half of the cases.

PATHOLOGY. The constant findings at autopsy have been subperiosteal hemorrhage in the diaphysis of the long bones, especially near the epiphyseal junction. There may be separation of the epiphysis and fracture. The hemorrhage may extend into the adjacent muscles and rarely into the knee-joint. There may be hemorrhages into the subcutaneous tissues, the mucous membranes, the skin, and more rarely into the viscera, particularly the spleen.

COMPLICATIONS. There is always a concomitant anemia and a general cachexia which increases with the duration of the disease and the internal or external bleedings. Enterocolitis and gastroenterocolitis are not infrequent complications. Fortunately the proper treatment of the scurvy usually has a marked beneficial effect on the intestinal condition. Most to be dreaded are the pulmonary complications, lobar pneumonia, and bronchopneumonia. Most of the fatal cases had pneumonia or succumbed to the progressive anemia and cachexia.

DIAGNOSIS. For diagnosis it is only necessary to keep in mind that scurvy does occur in infants, especially from seven to fourteen months old, and that its main features are pain, tenderness, and disability of the extremities, with swelling of the gums and a tendency to hemorrhage. If additionally there is the history of the child having been fed for a long time upon a sophisticated food or sterilized milk the diagnosis is certain.

DIFFERENTIAL DIAGNOSIS. The list of diseases for which scurvy has actually been mistaken is a long one; it is interesting that error in diagnosis has usually been made by a physician or surgeon working in some special field and seeing, consequently, few cases of infant feeding. The cases I have cited from my own records show early features which might have related to almost every type of specialist. Certain symptoms of scurvy in infants have been repeatedly mistaken for those of the following diseases:

1. *Rheumatism.* The fact that rheumatism is rare under two years of age, and almost unknown under one year, should be presumptive evidence against rheumatism in young infants. Moreover, in scurvy there is usually no fever or local heat in the swollen part, and the swelling is along the shaft of the bone primarily instead of in the joint.

2. *Rickets, especially Acute Rickets.* The intense pain, the swollen, bleeding gums, and the tendency to hemorrhage will indicate scurvy to be present even when there is coexistent rickets. The best of treatment is also of great aid in the differential diagnosis. In cases of scurvy and rickets the scorbutic symptoms disappear at once, while the rachitic symptoms persist for some months at least.

3. *Arthritis.* Gonococcic arthritis must be considered in the very young. Septic or pyemic arthritis must be considered if there is tenderness near several joints, and especially if there is profuse sweating. The correct diagnosis will be made upon careful physical examination, which shows the swellings to be in the shafts of the bone near the joint rather than in the joint or periarthritic structures. The condition of the gums will clinch the diagnosis.

4. *Paralysis, especially Anterior Poliomyelitis.* The drop-toe and loss of power are often suggestive; but the gradual development of the disability, the tenderness, the enlargement near the epiphysis, and the fact that the foot and leg can be moved, though reluctantly, show that the loss of motion is only the pseudoparalysis of scurvy.

5. *Syphilitic Epiphysitis.* On account of the epiphyseal swelling, tenderness, and pseudoparalysis, also on account of the frequent enlargement of the liver and spleen in scurvy, syphilitic epiphysitis is closely simulated. The preference of syphilis, however, is for the upper extremities, while scurvy usually affects the lower; moreover, the characteristic eruption of syphilis is absent, while the bruise-like marks, petechiæ, and swollen gums of scurvy are present.

6. *Sarcoma of the Femur.* Unfortunately there are many instances in which general surgeons have operated for sarcoma, when the swelling was unilateral, only to find a subperiosteal hemorrhage. The tenderness of the other limbs together, with the tumefaction of the gums, will correct the diagnosis.

7. *Osteomyelitis or Deep Abscess.* Goodhart and Still assert that the disability and swelling of the femur or the tibia has at times led surgeons to explore the bone for deep abscess. The longer history and the absence of fever, together with the swelling of the gums, should prevent this error.

8. *Purpura Simplex and Hæmorrhagica.* Purpura is to be distinguished by the absence of swelling of the long bones and of tenderness in the shafts of the bones

9. *Nephritis.* Since albumin with blood in the urine may be the first, and for a time the only, sign of scurvy the diagnosis of acute hemorrhagic nephritis has been made. The feeding history, together with the absence of fever, should make one suspicious. The tenderness, disability, and swelling of the extremities, together with the changes in the gums, confirm the diagnosis of scurvy. From nephritic œdema of the legs the differentiation is to be made by the absence of pitting on pressure, the disability of the legs, the great tenderness, and later by the changes in the gums.

10. *Dysentery; Ileocolitis, with Bloody Stools.* The diagnosis may be difficult, as in the case I have cited. The absence of fever, and of mucus or feces mixed with the blood, and the otherwise normal stools, will merely make one cautious about the diagnosis, until changes in the legs and gums occur.

11. *Intussusception.* At a discussion of this paper before the Hospital Graduates' Club of New York, Dr. J. F. Erdmann reported that he had been called one night by two physicians to operate for intussusception upon a child just under eight months of age. The child was apparently in a condition of shock, and was having cramp pains and bloody mucous stools. An exploratory operation seemed advisable, but during its course the infant went into collapse. While efforts at artificial respiration were being made, the gums were observed to be spongy and bleeding. The baby died. Further examination by daylight and close questioning into the previous feeding history proved without doubt that the child's bloody defecations were of scorbutic origin, no intussusception having been found upon operation.

In all the above cases, if the diagnosis is uncertain, the effect of treatment, the therapeutic test, is of the greatest value, inasmuch as the results show in forty-eight hours, and no harm can be done by waiting that long, as a rule. In a word, if in doubt, when the baby cries when the diapers are changed or the stockings are removed, stop the sophisticated food and give raw milk and orange-juice.

PROGNOSIS. The duration of scurvy is variable. If the faulty diet is continued without modification the child fails and dies of exhaustion or from some complication. When proper treatment is instituted improvement is almost miraculous. No results in medicine are more brilliant and none so easy to obtain. Within a comparatively few hours a pitiable, suffering little paralytic is transformed to a contented baby, waving its arms and legs in the sheer joy of living.

TREATMENT. Only a word needs to be said. The cause is to be removed. We are to stop the use of devitalized food, and to give fresh milk, fruit-juice (orange, grape, or pineapple), beef-juice, raw egg albumen, and purée of potato, according to the child's digestive capacity. In infants over a year old, purée of potato and of green vegetables is especially satisfactory. To discontinue the sophisticated food is often all that is necessary; but cure is more rapid when the fruit-juices are added.

Scurvy in adults is now almost a curiosity of medicine; it is dying out because understood. Its causes and treatment are recognized by the laws of all maritime nations, so that nowadays the disease is seldom seen even in the great seaports of the world.

A similar history of infantile scurvy is likely to obtain, and only sporadic cases appear almost as curiosities. This will not occur, however, until that distant day when infants are no longer fed on patent foods, but on fresh cows' milk that has been produced under ideal hygienic conditions. We shall still have cases of infantile scurvy until physicians, as well as the laity, realize that heating or boiling milk is not a physiological but a therapeutic measure. Recently Dr. Arthur Jacobus has informed me that much of the milk

sold in New York City by two of the milk companies has been already pasteurized or sterilized before delivery; this is done in order to evade the law against preservatives and the law against acidity or sour milk. Perhaps this fact may account for some of the cases of scurvy we see. To sterilize milk is often necessary, but it should be adopted rather as a mode of treatment than as a method of feeding; and it should not be continued indefinitely, any more than should arsenic, on the ground that it is a special form of food for the nervous system.

THE TREATMENT OF FRACTURE AND DISLOCATION OF THE VERTEBRÆ.

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Fracture of the spine, alone or accompanied by dislocation, while not an every-day occurrence, is still sufficiently frequent in the experience of men actively interested in traumatic surgery to merit a discussion of its treatment. The question of operative interference is also an open one and the results of such interference seem to vary to a considerable degree. There seems to be altogether too much tendency on the part of surgeons to look upon the injury, when severe, as necessarily fatal, and to decline to operate on the ground that they are "surgeons, not executioners," a sentiment that is utterly detestable to the chances of progression along this line of work.

During the course of the past summer two cases came under my care which presented some extremely interesting and instructive points, and which led me to inquire into (1) the degrees of injury to the spinal cord which we may assume to exist with different degrees of injury to its bony envelopment, and (2) the cases as they appear clinically.

The Pathological Condition. Presuming a fracture to exist the following seems to be a reasonable classification of the resultant conditions:

Pathological Class I. Fractured fragments slightly or not at all depressed; membranes and cord not injured.

Pathological Class II. Fractured fragments depressed; membranes torn, with hemorrhage about the cord, but no injury to the cord itself.

Pathological Class III. Fractured fragments considerably depressed, or the fracture accompanied by dislocation; membranes

lacerated, hemorrhage about the cord, contusion of the cord itself, and slight hemorrhage into its substance.

Pathological Class IV. Fractured fragments much depressed and usually accompanied by dislocation; lacerated membranes, hemorrhage about the cord, severe laceration of the cord itself, with hemorrhage into its substance.

Pathological Class V. A combination of the above conditions in which the dislocation is the more prominent feature and in which the cord is caught and compressed by the dislocated fragments, with or without contusion or partial laceration.

These divisions are made arbitrarily, differ principally in the degree of injury, and any of the conditions may exist as the result of direct or of indirect violence.

The factors in the foregoing conditions which are productive of symptoms and the symptoms they produce are these:

1. *Laceration of the cord,* causing an immediate loss of the power of movement, or sensation, or both.

2. *Compression of the cord,* causing a gradually increasing loss of the functions of movement or sensation, or both; this compression itself may be either (*a*) immediate, due to a bony deformity established at the time of injury, or (*b*) delayed, due to the action of an unchecked hemorrhage started at the time of injury. If the former, there is very little interval between the time the injury is received and the beginning of the onset of cord symptoms; if the latter, this interval may be long or short, but is always present.

3. *Laceration and compression of the cord,* producing the immediate symptoms of laceration combined with the more tardy symptoms of compression.

Hence we may assume that a case of severe back injury, in which the patient presents the symptoms of cramps in the legs, burning and tingling of the skin of the legs, followed by an increasing loss of the functions of movement and sensation in those parts, is a case of compression of the cord. Again, if a man with a fractured or dislocated spinal column has immediate loss of motion and sensation in his legs, we may safely say that such a symptom-complex points accurately to laceration of the cord. Finally a patient who presents the symptoms of immediate motor paralysis of the legs, followed by a gradual loss of sensation in the paralyzed parts, is clearly one in which there has been laceration of the motor area and compression of the part presiding over the function of sensation.

Thus the cases as they appear clinically divide themselves for our consideration into three classes:

Clinical Class I. Pure compression cases, that is, those which present the history of injury to the vertebral column, and locally the signs of fracture or dislocation, followed at an interval by an increasing paralysis.

Clinical Class II. Pure laceration cases, that is, those which present the unmistakable signs of fracture or dislocation, accompanied by immediate loss of sensation and power of movement of any or all structures whose site of spinal-cord control is located at or below the point of injury.

Clinical Class III. Combination cases, that is, those which, together with the gross signs of structural injury, show an immediate loss of sensation or power of movement, followed by a progressive loss of the functions not immediately destroyed.

TREATMENT. A careful consideration of the mechanics of the conditions likely to be present, and the mechanical means we have for their correction, will point the way to proper treatment.

Compression cases may owe their symptoms to one of several gross mechanical conditions:

1. Immediate bony compression may be due to (*a*) dislocation or (*b*) depressed fractured laminæ.

If due to dislocation we have the remedy in our hands: an open operation with suitable manipulation will reduce the dislocation and relieve the compression. If due to fractured and depressed laminæ, the offending fragments may be raised or removed entirely, at the discretion of the surgeon.

2. Delayed compression may be due to hemorrhage (*a*) about the cord or (*b*) into the cord.

In the former case the bleeding would naturally come from the vessels of the membranes and would create compression by its limitation by depressed laminæ: the remedy suggests itself, and a proper laminectomy together with control of the hemorrhage will afford the relief desired. In the latter case the hemorrhage into the cord would be, in all probability, merely one of the several factors entering into the general aspect of those cases which I have designated as combination cases.

Laceration cases, pure and simple, exist, from the standpoint of treatment, only when the cord is torn completely across, and all sensation and power of movement of structures physiologically below the particular segment under suspicion, are immediately abolished. Such cases are nearly always rapidly fatal and require the exhibition of such purely humanitarian methods of treatment as are afforded by the proper use of morphine. A condition of total cord destruction, at any level, justifies non-interference. Any injury to the cord of a less extent does not, in my opinion, carry with it any such justification whatsoever.

The combination cases are the most interesting, inasmuch as they present great opportunity for the saving of life, and, in addition, are those most frequently met with. Here we have a deformity produced which is of such a character that part of the cord is immediately lacerated and the remainder compressed. The duty of the surgeon is plain. We are powerless to repair the destroyed area. Suture of

the cord is beautiful in conception but, unfortunately, absolutely worthless in practice. Compression can be relieved, and an open operation in which the surgeon attacks mechanical difficulties with mechanical means will remove the factor of compression and allow the uninjured portion of the cord segment to regain its functional activity.

Thus far I have purposely avoided discussion of the special advisability of operation in cases in which the injury affects certain different regions of the cord. I believe that any case into which the factor of compression enters, or may be expected to enter, should be operated upon, and I do not believe that the special segment of the cord involved should influence the surgeon either for or against operation. An injury to the cord even at the level of the lowest dorsal vertebra is surely sufficiently grave to require surgical intervention, and the higher the location of the injury the greater the demand for the relief which operation alone affords. The location of the injury affects prognosis seriously, but not indications for treatment. Finally, as regards the time of operation, delays are dangerous, perhaps fatal. The necessity for accurate diagnosis does not exist. By all means operate at once.

The following is a brief record of the first case I have to report:

John M., aged forty-three years, a plumber by occupation, while at his work August 13, 1906, fell twenty feet from a scaffolding, and struck upon his head. He was rendered unconscious. An ambulance surgeon applied suitable dressings to his several injuries and transferred him to Fordham Hospital.

He was admitted at 6 P.M., put to bed, and examined by a member of the interne staff. There were several large lacerated scalp wounds, under one of which, in the occipital region, was a linear fracture of the vault of the skull, which was not depressed, but which apparently ran to the base. In addition he had a simple fracture of the left patella. He was conscious and rational, generally contused, in shock, and complained of great pain in the neck and lower limbs. He was catheterized and three ounces of clear urine obtained. His numerous wounds were dressed, splints were applied to his injured leg, and then, unfortunately, his spinal injury was overlooked; he was given morphine and went to sleep. Upon admission his temperature was 98°, pulse 88 and small, and respirations 26.

He was next seen about 9 A.M., August 14, fifteen hours after his accident, and was found to have entire motor and sensory paralysis extending downward from a horizontal line two and one-half inches below the clavicles; complete anesthesia of the skin of both arms except over an area corresponding to the deltoid muscles; paralysis of the extensor muscles of both arms and forearms; a tendency to tonic contractions of the flexor muscles of the arms; and a fracture of the base of the skull was evidenced by extensive double subconjunctival ecchymosis. His respirations were entirely diaphrag-

matic and he had paralysis of the bladder and the rectum, evidenced by urinary continence and anal relaxation. All reflexes over the area of anesthesia were abolished.

I first saw the patient at 2 P.M. August 14, and found him in the condition indicated above. At that time his temperature was 102°, pulse rate 100, and respirations 30. His face had the peculiar waxy, expressionless appearance common to cases of spinal-cord injury, and he was exceedingly weak. He had pain in his contracted biceps muscles and in his neck; otherwise he was without sensation of any sort. It looked as though the man had but an hour or two to live; temperature increasing, respirations becoming more rapid; he was weakening rapidly. It was already twenty hours since he had received his injury. He had, in addition, a serious head injury, and altogether the case appeared absolutely devoid of hope. I felt it was my duty to let him die in peace. He received stimulation of various sorts, and in the morning of August 15 his condition was markedly better. It was decided to give him what chance he had.

At 10 A.M., forty hours after his injury was received, he was put on the operating table in a right lateroprone position, and chloroform administered. I made an incision five inches in length with its centre over the fifth cervical vertebra and carried it down to the spinous processes. The muscles were freed and retracted laterally, giving a good exposure of the spinal column. There was fracture of the spinous process of the fourth cervical vertebra, and a dislocation forward and downward of its body upon the body of the fifth cervical. The fractured spinous process was removed, together with a portion of its corresponding lamina, with rongeur and chisel. There was a small rent in the membranes and no subarachnoid hemorrhage. By the removal of the portion of the lamina I had established a point upon which I could exert leverage.

One assistant was delegated to make traction upward upon the head, another to press backward upon the throat, and a third to press downward directly upon the spinous process of the fifth cervical vertebra. When all were ready, I inserted a curved periosteal elevator into the spinal canal, between the membranes and the posterior portion of the canal formed by the dorsal parts of the fourth and third cervical vertebræ, and at a signal we all "heaved together," and the dislocation was reduced without any trauma to the cord itself. All bleeding was checked, the muscles were drawn together slightly in the median line by interrupted catgut sutures, the fascia united with a running suture of chromic gut No. 2, and the skin closed with silkworm-gut and silk. A small rubber-tissue drain was introduced to the site of fracture. A cast was immediately applied to his head and shoulders, and the patient was placed upon a water-bed. The time required for operation was forty-five minutes, and the patient left the table in better general condition than when he was put upon it.

He recovered consciousness in about twenty minutes and immediately began to move his arms. He had regained sensation over the entire dorsal surface of his arms and forearms and also over a small area corresponding to the middle third of his biceps muscles. There was a noticeable improvement in the depth and character of the respirations, and the tonic spasms of the flexor muscles of his arms were no longer present.

In two hours his temperature had reacted to 100° and his pulse was 100 and of fairly good character. From this point on he gradually became weaker, and died, eight hours after operation, of respiratory paralysis, his heart continuing to beat for several minutes after respiration had apparently entirely ceased. No autopsy was had.

This case seems to me to be one of pure compression. He certainly had no laceration of the cord, else we would have had some immediate evidence of it at the time of his admission; that there was no hemorrhage about the cord I demonstrated at the time of operation. The deformity was very marked and was easily sufficient to have caught the cord and gradually squeezed out its life. I cannot help feel that, had this patient been carefully watched and the first symptom of compression noted, operation at that time would undoubtedly have saved the man's life, and in all probability have restored him to complete functional activity.

My second case has had a more fortunate termination, and this in spite of the fact that his injury was more severe. The history is as follows:

Joseph D., about thirty-five years old, a carpenter by trade, was leaning out of a window of a building then in the course of construction, when he was struck on the back by an iron beam which weighed about three hundred pounds and which fell ten feet. He dropped back into the room unconscious. He regained his senses almost immediately and found himself unable to move his lower limbs. An ambulance carried him to Fordham Hospital. His temperature on admission, August 28, 1906, at 9 A.M., was 99°, his pulse 96, his respirations 32.

lower part of his abdomen and in the thighs, legs, and feet, and intense pain in his back. On a line with the tenth rib there was a depression in the median line of the back, and a point of great tenderness.

I saw the patient at 10.30 A.M., two hours after the accident. He was in about the condition described above except that the anesthesia was becoming more complete. I advised operation. At 1 P.M. the patient was very weak, temperature 97° by rectum, pulse 72 and very small, and respirations 26. He was completely anesthetic from the umbilicus down. At 2.30 P.M. he consented to operation. Immediately before he was put upon the table he was again catheterized and four ounces of bloody urine was obtained.

At 3 P.M., six hours after the time of the injury, he was taken to the operating-room, placed upon the table in a right lateroprone position, and chloroform was administered. I made an incision six inches in length, in the median line of the back, with its centre over the depressed area. Cutting down to the spinous process the muscles and fascia were found ecchymotic. At the situation of the ninth dorsal vertebra there was a marked depression in the line of the spinous processes and those belonging to the eighth, ninth, and tenth dorsal vertebræ were evidently broken. The last two ribs on the left side were broken and the end of the twelfth rib was jammed into the region of the kidney on that side; the tenth dorsal was dislocated forward upon the ninth. Attempt at reduction at this point was defeated by impaction of the fragments. I removed the spinous processes of the tenth and ninth vertebræ, together with their corresponding laminæ, and found the membranes torn to pieces. From the position of the spinal cord it was evident that it had been pressed upon by the fractured laminæ just removed, and it appeared to be contused. My second attempt at reduction by manipulation and traction by means of strong bullet forceps, applied directly to the vertebral body of the tenth dorsal, was successful.

With the bodies of the vertebræ in line, the spinal cord in its proper place, and compression due to secondary dislocation guarded against by the removal of the laminæ of the tenth and ninth dorsal vertebræ, I considered that I had done all that could be done at that point. The region of the wounded kidney had ceased bleeding. The wound of operation was rendered as dry as possible, and the right and left erector spinæ muscles were drawn together in the median line with interrupted sutures of catgut. The fascia was sutured with chromic gut No. 2, and the skin closed with sutures of silkworm-gut and silk. A small rubber-tissue drain was inserted at the middle of the incision and carried down to the point of fracture. The patient left the operating-room in good condition and was immediately put upon a water-bed. The time required for operation was sixty-five minutes.

He rested nicely that evening and night, and the following day

I applied a plaster cast to his body, extending from the axilla to the knees, and removed the rubber-tissue drain. The experience of putting on the cast was very painful and trying for him, and during the time required for its application his pulse gradually quickened until it reached 180 to the minute. He also complained of great precordial pain. Hence his condition twenty-four hours after operation was not encouraging. His temperature was 102°, pulse 180, respirations 36. The urine contained much blood; twenty ounces in twenty-four hours by catheter. He was being vigorously stimulated, chief reliance being placed on saline and whiskey enemas, and strychnine hypodermically.

On the third day his condition was unchanged.

On the fourth day he was improving; by the eighth day his temperature was 98°, his pulse 92, and his respirations 20. Twenty-six ounces of pale, pinkish urine was obtained by catheter in twenty-four hours.

From this time there was no change until the tenth day, when he began to have irregular sensations of pressure and tingling in his legs and thighs.

On the eleventh day his general condition was good. He began to have painful sensations in his legs.

Later notes are as follows:

Fifteenth day. Wound dressed and found absolutely clean, with no stitch infection. Sensations better and improvement in left leg more rapid than in right. Urine now clear and normal in amount. Bowels moving after enemas. Catheter still necessary.

Ninteenth day. Patient beginning to have a little irregular temperature, since seventeenth day. Has slight cystitis. Bladder irrigations of boric acid twice daily.

Twentieth to twenty-eighth day. Cystitis has not grown any worse, but temperature has gradually increased in severity during the past week. Wound examined today and several spots of budding granulations along its course discovered. Apparently catgut infection. Openings slightly enlarged.

September 29, 1906, twenty-ninth day. Temperature normal. The cystitis is somewhat troublesome and tends to grow worse.

September 30. Patient anesthetized and an external urethrotomy done. Continual drainage afforded.

October 2. Patient in good condition. Cast removed.

Since that time the patient has steadily improved. Sensation is good in his entire left thigh, leg, and foot. His right thigh has some irregular spots where the sensation is not good. With the exception of these he has entirely regained his normal power of feeling. Motion has never shown any tendency to return. His skin is well nourished and there is remarkably little muscular atrophy. His wound of operation is entirely healed. His perineal wound is clean and granulating. He is not able to void urine. He feels well and looks well.

November 6. Patient was allowed to sit up in bed, and did so without experiencing any discomfort. In spite of the fact that he is paralyzed from his waist down, as far as movement goes he is particularly pleased with the fact that he is alive.

In regard to the operation itself there are some points which suggest themselves:

1. Nothing is gained and time is lost by a small incision.
2. No more bone should be removed than is absolutely necessary to provide proper exposure of the cord and a reduction of the dislocation.
3. If the membranes are found intact an aspirating needle will demonstrate the presence of blood beneath, and the membranes should not be incised needlessly.
4. The membranes should be closed, if possible, with a fine catgut or silk suture.
5. Drainage should be provided for any oozing that may take place from the wound of operation. A rubber-tissue drain is sufficient for this purpose and should be removed at the end of twenty-four hours.
6. An immediate external urethrotomy should be done and continual drainage provided for the bladder.

THE MOST FREQUENT HERNIA IN CHILDHOOD AND ITS SIGNIFICANCE.

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In 1904 I expressed my belief that the majority of herniæ in children are acquired and not congenital. Since then I have continued my study of the subject, but unfortunately have been obliged to delay until now the publication of the data bearing on the subject I have accumulated.[1]

If one turns to the work of those who regard these herniæ as being of congenital origin, and therefore often requiring active surgical interference, it is obvious that they take as the standard of their authority the fact that they have performed so many tens or hundreds of operations for the condition. Indeed, it is usually stated so in the early paragraphs of their papers. This is a very narrow point of view, which might almost be compared to an attempt to examine a landscape through a microscope instead of a telescope.

[1] Lancet, August 20, 1904; later communications: International Clinics, 1905, ii, 15th series, p. 154, and Medical Review, 1905, viii, p. 569.

The problems of the origination of herniæ in children cannot be settled only by observations made at the operating table. Careful notes and records in the out-patient room should come first, and the results obtained in this way should be examined and checked in the operating theatre. It will then be found that there is a close relationship between the conditions of the parts noted in the theatre and certain facts in the clinical history observed in the out-patient room. Thus it becomes possible to understand and interpret the character of the cases.

With the aid of my clinical assistants, especially Mr. Howell Evans and Dr. Irving Pinches, a survey was made of the herniæ in the out-patients at the Great Ormond Street Hospital, who attended on my days. To these two gentlemen I owe many thanks for the work they have done. When we had completed about seven hundred observations it was felt that we had omitted to include a most important factor and that the whole work should be repeated. The results of this collective investigation of the first series are summed up in the accompanying table:

I. FIRST SERIES OF 700 OBSERVATIONS.

	Per cent.
Right inguinal hernia	38.3
Right and left inguinal herniæ	10.8
Right and left inguinal and umbilical herniæ	8.0
Right inguinal and umbilical herniæ	12.0
Left inguinal herniæ	10.6
Left inguinal and umbilical hernia	2.7
Umbilical herniæ	16.2
Epigastric hernia	0.9
Femoral, right and left	0.15
Complicated by a ventral hernia between the divaricated recti	14.3
Single herniæ	66.0
Multiple	34.0

The above includes all the ordinarily recognized herniæ, but no account is taken of the median ventral hernia between the upper parts of the recti abdominis muscles, except that it was noticed casually that 14.3 per cent. were accompanied by this ventral hernia. But as more and more observations were made, becoming convinced of the importance of this missing factor, we terminated the investigation after seven hundred observations had been made, and commenced a new inquiry on a wider plan and executed by a larger number of helpers, whose observations were "untainted" with my particular opinions on the subject. All concerned in this second investigation except myself were ignorant of the figures and fallacies of the first investigation, so that their observations were unbiased.

One very remarkable fact was shown by the first investigation; namely, that multiple herniæ are far more frequent in children than they are in adults. Single herniæ were found in 66 per cent.;

multiple herniæ in 34 per cent. This is suggestive either of the multiplicity of congenital sacs in one subject or of one factor which was the common cause for the herniæ present. But it was obvious that this survey was very incomplete, because we had omitted to take into consideration, as almost all previous authors have, the hernial protrusions between the divaricated recti.[2]

Like herniæ in other parts of the body, the ventral hernia between the divaricated recti is not necessarily obvious unless the abdominal muscles are thrown into action, such as is done when obtaining the impulse on coughing in adults. To do this in children requires some little skill and tact, so that the observations are not often made. The most generally applicable method is to place the child on its back on a table or its mother's lap; often it will begin to cry at once—when the ventral hernia will become obvious. If this is not so, its abdominal muscles may be stimulated by a finger or the handle of a pen. Should this fail, as it often does, the child's head should be supported with one hand, which at first raises it and then allows it to fall sharply backward two or three inches. Whilst this is being done the observer should watch the abdomen for the momentary contraction of the muscles; a carinate projection appears above the umbilicus if a median ventral hernia is present. In difficult cases other means may be required to demonstrate the protrusion. If care is taken, I believe that this hernia will be found more frequently than is indicated by my collective investigation of 2600 cases, in which it was noted in 24.21 per cent. In fact, one knows that the more carefully the observations are taken the more frequently will a median ventral hernia be found. For instance, two of those who helped me found the median ventral hernia present in 63 per cent. and 21 per cent. respectively, showing that the results vary with the observer, possibly depending on both the care and the time spent in making them.

Sir Frederick Treves[3] has stated that the sac, its coverings, and its contents are the three essential parts of a hernia. Recognizing that a hernial sac does not always contain viscus, a hernia may be recognized as being formed of a peritoneal protrusion which has separated some of the structures which form the abdominal walls; the formation of the peritoneal sac may or may not be accomplished by some abdominal viscus or viscera.

[2] As my object was to obtain, in the second and larger survey, results independent of my private views I asked many to help. To them I must acknowledge my thanks: Dr. A. F Stabb, Obstetric Physician to St. George's and Queen Charlotte's Hospitals; Mr. G. E. Waugh, one of my surgical colleagues at Great Ormond Street; Mr. H. A. T. Fairbank, another of my surgical colleagues at Great Ormond Street and attached to Charing Cross Hospital; Mr. Howell Evans, of Great Ormond Street and Children's Invalid Aid Association, and Dr. Irving Pinches, my clinical assistants; Mr. Duncan Fitzwillian, Casualty Officer to Great Ormond Street; Dr. S. R. Gibbs, Mr. H. T. Gray, and R. T. H. Cox, of St. Thomas' Hospital; Dr. Vowe Johnson, of the Lambeth Schools Infirmary, and particularly Dr. Cursham Corner, for large and invaluable series of observations on the newly born.

[3] Text-book of Surgery.

Naturally these protrusions occur at the weaker regions of the abdominal walls: the inguinal, femoral, and umbilical regions. When the recti muscles are divaricated, the linea alba is stretched and thinned, allowing the peritoneum and perhaps the omentum and intestine to bulge forward. This bulging constitutes a true hernia having all the essential parts; and, as it is found almost exclusively in children, it is a peculiar character of their herniæ. Because it was neglected, my first series of observations which extended over two years and more was invalidated, and the second series was undertaken to remedy the defect.

As with all other herniæ, the median ventral hernia between the divaricated recti may be congenital or acquired. Differing from inguinal and femoral herniæ in the sac having no neck and communicating widely with the abdomen, its presence is demonstrable with its first appearance, which need not be so in cases of the others mentioned. The observations of Dr. Stabb and Dr. Cursham Corner have shown that it is a very uncommon, but not unknown, condition to find in the newly born; the former found it only once in 122 observations. Hence, there is little evidence in favor of its congenital origin. How then can it be acquired? As any given child can only digest and absorb a certain amount of nutriment, which varies with its every mood, any residue, whether an excess of good food or the remains of an indigestible meal, will "go bad" and ferment in the intestine unless expelled. For details of its fermentation I must refer the reader to another paper.[4] In this place it need only be stated that, amongst other products, gases are formed which distend the intestines, raise the intra-abdominal pressure, and, if not quickly got rid of, will dilate the belly, separating the component parts of its walls. To particularize the subject of communication, the ventral herniæ between the upper parts of the divaricated recti appear for two reasons: first, as the direct result of the increased intra-abdominal pressure; and second, as the indirect result of the continuance of the raised pressure upon the growth of the tissues of the linea alba.

The incidence of this ventral hernia at the different ages of life is of great interest. I am indebted to Dr. Cursham Corner for his observations in the early stages of life. He remarked that, on the average, the umbilical cord separated on the fifth day; when there was invariably some bulging of the umbilical cicatrix which lasted until the eighth day, when the scar became firm. The size of the bulging was dependent upon the length of cord left proximal to the ligature. He made 201 observations on children between birth and one year of age and found a median ventral hernia between the divaricated recti in 18.5 per cent., being more frequent amongst the older infants. At Queen Charlotte's Hospital, Dr. A. F. Stabb

[4] Some Surgical Results of Improper Feeding. Clinical Journal, June 27. 1906, p. 171.

found only 1 case[5] of bulging between divaricated recti amongst 122 infants varying from one to thirty-nine days old. Amongst other observers, at the Great Ormond Street Hospital, bulging between divaricated recti was found in 34 per cent. of infants under six months of age and in 58 per cent. between six months and one year of age. These figures may be arranged as follows:

	Per cent.
Queen Charlotte's Hospital (1 to 39 days)	0.8
East End Mothers' Home (1 to 365 days)	18.5
Great Ormond Street Hospital (under 6 months)	34.0
Great Ormond Street Hospital (6 to 12 months)	58 0

II. INCIDENCE OF A MEDIAN VENTRAL HERNIA BETWEEN THE DIVARICATED RECTI AT DIFFERENT AGES.

Years	Ventral herniæ.
1	30.0 per cent.
2	62.7 "
3	50.0 "
4	47.8 "
5	43.5 "
6	40.2 "
7	30.9 "
8	28.8 "
9	17.7 "
10	20.0 "
11	17.3 "
12	11.8 "
13 and 14	8.7 "

This table shows that the frequency of the median ventral hernia increases steadily from birth to attain its maximum in the second year of life; then it falls steadily until adult life is reached, when it is rarely seen. Therefore, it would appear that a median ventral hernia between the divaricated recti is an acquired character which becomes spontaneously cured as growth takes place. Its significance in connection with the formation of inguinal hernia is enormous. If one sees a house on fire and finds one story alight, it is natural to conclude that some incident has occurred which originated the fire. But if one finds two, three, or more stories alight, one concludes that they arose from one common cause and not that there were two, three, or more simultaneous fires kindled. Hence, if we find multiple herniæ, as in Table I, at least we may suspect that they have a common causation, though there is no proof that they are not all of congenital origin. But when in addition they are combined with a median ventral hernia between the divaricated recti, as in Table III, an acquired character known to be due to the raised intra-abdominal pressure, the probability is greater that they have a common and a similar origin. Thus, this form of ventral hernia becomes an indication of extreme etiological importance. In Table III is represented

[5] An infant one day old.

the percentage in which the presence of this ventral hernia was found at the different ages.

III. SECOND SERIES OF 2600 OBSERVATIONS.

	Of all cases.
Herniæ present in	32.7 per cent.
	Of all herniæ.
Right inguinal hernia	4.2 per cent.
Right inguinal hernia and median ventral hernia between the divaricated recti	4.7 "
Right inguinal and umbilical herniæ	0.8 "
Right inguinal and umbilical herniæ and median ventral hernia through the divaricated recti	2.3 "
Left inguinal herniæ	1.3 "
Left inguinal herniæ and median ventral hernia through the divaricated recti	2.1 "
Left inguinal and umbilical herniæ	0.4 "
Left inguinal and umbilical herniæ and median ventral through the divaricated recti.	0.5 "
Umbilical herniæ	4.2 "
Umbilical herniæ and median ventral hernia through the divaricated recti	13.3 "
Median ventral hernia between the divaricated recti	61.3 "
Right and left inguinal hernia	1.0 "
Right and left inguinal herniæ and median ventral hernia through the divaricated recti	1.4 "
Right and left inguinal and umbilical herniæ	0.1 "
Right and left inguinal and umbilical herniæ and median ventral hernia through the divaricated recti	1.5 "
Epigastric herniæ	0.9 "

The median ventral hernia was found by itself in 61.3 per cent. of the cases of hernia; and when in combination as well, in 87.1 per cent.—a very strong indication of the probable origin of a very large number of the concomitant inguinal herniæ, and, as the congenital causation of them in certain cases is not disputed, of the composite, not simple, causation of herniæ.

This is strikingly brought out by the following figures which represent the percentage proportions amongst the various herniæ found. In Table V the herniæ accompanied by the ventral hernia between the divaricated recti is just twice as large as when unaccompanied—a fact which would suggest that pressure herniæ, that is, acquired, are twice as common as herniæ of congenital origin.

IV. FROM THE SECOND SERIES.

	Per cent.
Of all the 2600 cases of herniæ were found in	32.7
Median ventral hernia through the divaricated recti (with and without other herniæ)	24.21
Herniæ other than those between the divaricated recti	15.4
Herniæ unaccompanied by one between the divaricated recti	4.62

V. OF THE HERNIÆ THEMSELVES.

	Per cent.
Hernia accompanied by a median ventral hernia through the divaricated recti	25.8
Hernia unaccompanied by a median ventral hernia through the divaricated recti	12.9
A median ventral hernia through divarication of the recti; present alone	61.3
A median ventral hernia through divarication of the recti; alone and with other herniæ	87.1

Every variety of hernia is more common when associated with another between the divaricated recti than when alone or associated with any other variety of hernia.

There are two main theories of hernia formation: one, ably and vigorously advocated by many surgeons, amongst whom may be mentioned Mr. Stiles, of Edinburgh; Mr. Carmichæl, of Edinburgh; Mr. Murray, of Manchester; Mr. Clogg, of London, and especially Mr. Hamilton Russell, of Melbourne, who has named it the saccular theory, infers that herniæ appear on account of the sac being formed during development; the second, I believe first suggested by Mr. Arbuthnot Lane, in 1897, and amplified by me in 1904, in which it is argued that the majority of herniæ in children arise from the increased intra-abdominal pressure which results from the gas production of intestinal fermentation. On the latter theory, the hernia can be produced in either of two ways, or by a combination of both: first, the intra-abdominal pressure may protrude the hernia by direct pressure; second, and more commonly, the pressure acts indirectly by modifying the growth of the tissues, particularly in the weaker regions, facilitating the development of a hernia by direct pressure later. By the indirect action on its growth, the raised intra-abdominal pressure destroys the protective valvular action of the inguinal region, after which a hernia is formed. In very young children the valvular action may be rendered incompetent by the mere stretching of the soft growing tissues. Thus, the younger the child the shorter the time required for the development of a hernia. But the mere presence of a hernia in a child shortly after birth does not necessarily indicate its congenital origin; for instance, it is known even with the tougher tissues of adults that a hernia may appear in a few hours or days.

To recapitulate, a median ventral hernia between the upper parts of the divaricated recti is manifold the most common and characteristic hernia of childhood. Its importance has not been recognized owing to the fact that surgeons have made more observations in the operating theatre than in the out-patient room, and have, with few exceptions, never combined these two sets of observations. This median ventral hernia is almost invariably an acquired character and is directly related to the pressure of gas production

by intestinal fermentation. Any hernia or set of herniæ in any situation is more frequent when accompanied by it than when alone (Tables III and V). Hence clinical experience shows that raised intra-abdominal pressure is directly related to the frequency of inguinal herniæ, and, it is suggested, probably also to their initiation. It has been further suggested that the true proportion of acquired to congenital herniæ is about 2 to 1 (Table V).

In the face of the fact that it is nearly impossible to recognize and distinguish the funicular variety of the congenital hernial sac from the acquired sac at an operation and even perhaps at a necropsy, there can be no certain knowledge of the formation of herniæ in children. Therefore, I would suggest that by means of the recognition of the presence and significance of the median ventral hernia, its frequency and associations, it is possible to introduce a strong probability into the question, which would seem to indicate that acquired herniæ are more common in children than those due to the presence of a congenital sac. This is not a mere academic question, as the line of treatment to be adopted must depend largely upon its appreciation.

THE CLINICAL RESEMBLANCE OF CEREBROSPINAL SYPHILIS TO DISSEMINATED SCLEROSIS.[1]

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The diagnosis between cerebrospinal syphilis and multiple sclerosis, while not usually regarded as difficult, may in some cases be very perplexing. Both multiple sclerosis and syphilis vary in their symptomatology according to the location of the lesions, so that difficulties in clinical diagnosis might be expected. In this paper no special reference is made to those cases of disseminated syphilitic lesions which resemble multiple sclerosis pathologically as well as clinically, nor is any possible causal relationship between the two diseases discussed.

A case in which a positive diagnosis between cerebrospinal syphilis and multiple sclerosis for a long time seemed impossible

[1] Read at a meeting of the Philadelphia Neurological Society, January 22, 1907.

was under the care of one of us (Dr. Spiller) during several of his terms of service in the Philadelphia General Hospital, and was frequently presented in lectures to the students as probably one of multiple sclerosis. The patient died two weeks after the termination of one of these terms of service, and we are, therefore, indebted to Dr. James Hendrie Lloyd for the pathological material.

P. B., aged twenty-eight years, was admitted to the Philadelphia General Hospital November 10, 1902, complaining of tremor, difficult locomotion, and a steady, constant pain in the legs just above the knees.

His father was living and well; his mother was dead of an unknown cause. Three brothers and one sister were living and well. The patient was married and the father of one healthy child. He admitted having had gonorrhœa when fifteen years of age and chancroid when about twenty years of age, but denied any history of syphilitic infection; subsequently, a few months before his death, he admitted having had syphilis. He denied excessive use of alcohol, and was always apparently strong and healthy. About six months previous to the onset of his present trouble he had his hands and feet frost-bitten while shovelling snow, but they were not much swollen, and he worked the next day as usual.

His present trouble began about two months before his admission to the hospital in 1902, when he noticed that when walking he would stagger and have pains in his legs. The pains were slight and not sharp or shooting in character. Three weeks after the legs were affected he noticed a beginning affection of the hands and arms, the nature of which is not recorded, unassociated with any pain, however. He stopped work about one week previous to his admission to the hospital, on account of repeated falls from his sweeping machine.

On his admission to the hospital it was noted that his gait was distinctly ataxic and that his station was very poor, so that he fell when he attempted to take the position of "attention" with his eyes open or closed. His irides reacted normally to light and in accommodation. He had general tremors of the limbs. His speech was affected and his tongue was tremulous. The knee-jerks were absent. Ankle clonus was slightly manifested and plantar irritation showed a slight extension of the great toe on the left side. The examination of the chest and abdomen was negative.

October 21, 1903. An ocular examination was made by Dr. E. A. Shumway; the ocular movements and the pupillary reactions were normal. Vision, O. D. $\frac{5}{20}$, O. S. $\frac{5}{15}$. The ophthalmoscope showed a pallor of the temporal half of the right optic nerve and a decided simple atrophy of the left optic nerve. The visual fields of both eyes were concentrically contracted, but especially that of the left.

November 12*th*. It was noted that the patient was exceedingly nervous and irritable. He did not have nystagmus. The upper

extremities showed a coarse tremor on movement and he was unable to button his clothing. He had slight loss of voluntary power, the dynamometer registering 50 in each hand. With his eyes shut, he recognized correctly familiar objects placed in his hands. The tendon reflexes were apparently lost in the upper extremities, but the tremor made the examination difficult. His gait was ataxic, and he could not stand unsupported with his eyes open or closed. The knee-jerks were lost. Ankle clonus was present on each side, but the Babinski sign was apparently present only on the left side. He had no loss of sensation.

February, 1905. It was noted that the knee-jerks and ankle clonus were absent on both sides; that there was a marked intention tremor of the hands and a staccato speech.

February 20. An ocular examination was made by Dr. Charles A. Oliver. The right pupil was larger than the left. Both irides were sluggish to light, but prompt in accommodation and convergence. The movements of the external ocular muscles were good in all directions. The papulomacular wedge and the tissues in the optic nerve, downward and outward, were partially atrophic. The left optic nerve was more diffusely atrophied than its fellow. Efforts to outline the visual fields were unavailing owing to the patient's mental condition.

March 10, 1906. Notes made by Dr. Wm. G. Spiller. His condition was much as it had been for several years, only the man was much weaker than he had formerly been. He had difficulty in showing his teeth, and when he attempted to do so there were irregular movements about his mouth of the character of an intention tremor. He wrinkled his forehead well on each side, but was unable to draw up either corner of his mouth separately. When he closed his eyes there was a tremor of the muscles above the eyelids. This intention tremor of the muscles of the face was very striking and was a new sign. The movements of the eyeballs were free and there was no nystagmus. Sensation for touch and pain was normal in the face. The tongue jerked violently backward and forward when he attempted to protrude it, but when at rest it presented no tremor. The tremor of the tongue was an intention tremor. The masseter muscles contracted well. Speech was very difficult, tremulous, and scanning. The upper limbs were not wasted and showed some small white scars, which the patient now confessed were caused by syphilis. The slightest voluntary movement of either upper limb produced marked intention tremor. Every few minutes he had involuntary jerkings of one or the other upper limb. The biceps tendon reflex and the triceps tendon reflex were lost on each side. Sensation to touch and pain seemed to be unaltered in the upper limbs. There was no wasting of the hands or of the trunk muscles. The grasp of each hand was feeble. The lower limbs were not muscular, but there was no localized atrophy. The patellar reflex

was completely lost on each side, even on reinforcement. The lower limbs could be moved in all parts, but the movements were feeble and intention tremor was pronounced in most of them. The tendo Achillis jerk was lost on each side. Babinski's sign was not distinctly present on either side, the movements of the toes being uncertain. Sensation for pain was normal in the lower limbs, but his answers regarding tactile sensation were unreliable because of his mental dulness. If not aroused he had a tendency to fall into a slightly stuporous state.

March 23. Mental aberration was present; he was delusional and swore considerable.

April 10th. He was somewhat quieter. Pulse rapid, but of good tension; temperature 101°; respirations increased in frequency and shallow. Examination of the chest was negative. He died on April 16, at 8 P.M.

At necropsy the brain and spinal cord appeared normal. They were removed and preserved in 10 per cent. formalin solution for histological examination.

In sections from the lumbar region of the spinal cord stained by the Weigert hematoxylin method, the posterior columns appeared much degenerated in the manner usually seen in tabes, the cornu-commissural zone and the oval field of Flechsig escaping. The lateral columns in the region of the crossed pyramidal tracts were a little less deeply stained than the rest of the anterolateral columns. Sections stained by acid fuchsin and hemalum showed round-cell infiltration of considerable intensity in the pia, but not about the bloodvessels within the spinal cord. The bloodvessels in the pia and those in the anterior roots were much congested and thickened. The nerve cells in the anterior horns stained by the thionin method were in a fairly good state of preservation, but here and there a very highly diseased cell was found.

The round-cell infiltration of the pia was more pronounced in the thoracic region than in the lumbar cord, and there was also a slight cellular infiltration about some of the bloodvessels of the spinal cord, especially in the sclerotic areas in the posterior columns. The posterior columns, except the cornu-commissural zones and along a part of the posterior septum, appear intensely degenerated in sections stained by the Weigert hematoxylin method. The crossed pyramidal tracts were a little less deeply stained than the rest of the lateral columns. The columns of Lissauer were degenerated.

In the cervical region the posterior columns were still intensely degenerated, and the degeneration resembled that of tabes. The lateral columns appeared to be normal. Round-cell infiltration of the pia was about as intense as in the lumbar region, but there was no distinct infiltration about the bloodvessels in the spinal cord. The nerve cells of the anterior horns were in about the same condition as those in the lumbar region; here and there a nerve cell was seen that was much degenerated.

Sections of the medulla oblongata stained by the Weigert hematoxylin method appeared to be normal. The hemalum-acid-fuchsin stain showed the round-cell infiltration of the pia to be as intense here as in the spinal cord, but it was not present about the bloodvessels within the nervous substance. Sections through the pons and through the cerebral peduncles showed the same round-cell infiltration in the pia, but the sections appeared otherwise normal. The cells of the nuclei of the hypoglossal, facial, abducens, trochlear, and oculomotor nerves, as well as the nucleus ambiguus, appeared normal when stained by the thionin method.

The pia of the right and left paracentral lobules was infiltrated with round cells and there was a distinct round-cell infiltration about the bloodvessels within the cortex. The cells of Betz appeared to be in a very fair condition, although here and there a cell was found partly degenerated.

Round-cell infiltration about the optic chiasm was only of moderate intensity, and was also found within the chiasm about the bloodvessels. The optic nerves and chiasm stained well by the Weigert hematoxylin method.

Sections of the cerebellum showed a moderate round-cell infiltration of the pia mater. Some of the Purkinje cells showed peripheral displacement of the nucleus.

The oculomotor nerves appeared to be partially degenerated and presented considerable round-cell infiltration within the nerves and an overgrowth of the connective tissue. Both sixth nerves appeared partially degenerated, when stained by the Weigert hematoxylin method, and there was considerable overgrowth of connective tissue within them. The motor and sensory roots of the left fifth, the left seventh, the left ninth and tenth, and the right twelfth nerves appeared fairly normal by the hemalum-acid-fuchsin and Weigert hematoxylin stains.

In order to show the resemblance of this case to one of multiple sclerosis it may be well to give a brief summary of it.

A young man positively denying, during several years, syphilitic infection, presented marked ataxia of gait, intention tremor of the limbs, and, a month or two before death, of the muscles of the face; scanning speech; at first normal iridic reactions, later Argyll-Robertson pupils, with unequal pupils; pallor of the temporal side of the right optic nerve and simple atrophy of the left optic nerve; and vertigo. Pain was never a prominent symptom. Remissions did not occur during the years he was in the hospital. Nystagmus was not observed. Shortly before his death, when some scars on his limbs were discovered and a history of syphilis obtained, the diagnosis of cerebrospinal syphilis was entertained, although it was not forgotten that a patient with multiple sclerosis is not exempt from syphilis.

The lesions found were those of meningo-encephalomyelitis, consisting chiefly of round-cell infiltration and degeneration of the posterior columns of the cord.

The patient was married and was the father of a healthy child. He positively denied having had syphilis until a short time before his death; on the other hand, his occupation, in which he was constantly exposed to the weather, and a history of having had a severe exposure to cold a short time before the onset of his illness, furnished a possible etiology for multiple sclerosis. The influence of exposure to cold and damp in the causation of multiple sclerosis has been referred to by Krafft-Ebing, Spiller, and others. Pain was never a marked feature of the case, and at no time was of the sharp, shooting character usually associated with inflammatory lesions of the meninges involving the posterior roots. The attacks of vertigo, as indicated by the repeated falls from his sweeping machine, are also in favor of the diagnosis of multiple sclerosis.

The gait in many cases of spinal syphilis, as also in multiple sclerosis, is of the spastic-paretic type, but the ataxic type is common. In this case there was marked ataxia in gait and station, which, however, was not increased by closing the eyes, so that it resembled the incoördination of gait characteristic of multiple sclerosis. The tremor was of the so-called intention type, was widely distributed, and involved, late, the tongue and the muscles of the face as well as the limbs. This intention tremor is regarded generally as being diagnostic of multiple sclerosis. The speech was "scanning," but there was no nystagmus. Uhthoff[2] found nystagmus present in only 58 per cent. of cases of multiple sclerosis, so that its absence in this case was not regarded as particularly significant. In six cases observed by E. W. Taylor,[3] in which the diagnosis was confirmed by necropsy, nystagmus seems to have been observed in only one or two, and then only on lateral deviation of the eyeballs. Uhthoff calls attention to the analogies between the ocular changes that occur in cerebrospinal syphilis and those of multiple sclerosis; the frequency of visual changes without ophthalmoscopic findings and recovery from them, the unilaterality of the symptoms, with the great infrequency of double total blindness. The changes in multiple sclerosis are of a less severe grade than those of syphilis; hemianopsia is rare; ophthalmoscopic changes are less marked and may last longer without alteration of vision. Optic neuritis is relatively seldom found in multiple sclerosis. A simple atrophy and pallor occur in both diseases. Parinaud[4] calls attention to the fact that paresis of a single eye muscle ending in recovery is frequent in multiple sclerosis, while complete or lasting paralysis rarely occurs, which it does, however, in syphilis. The findings in our case of a

[2] Archiv f. Ophth., Band xxxix, Heft 1 und 3.
[3] Journal of Nervous and Mental Disease, June, 1906.
[4] Progrès méd., August, 1884.

simple atrophy of one optic nerve and an atrophy limited to the temporal half of the other were very suggestive of multiple sclerosis.

The knee-jerks and the Achilles jerks are usually exaggerated in both multiple sclerosis and cerebrospinal syphilis, but this symptom depends on the location of the foci of the disease, and as has been shown by one of us (Spiller[5]), the knee-jerks may be lost in multiple sclerosis if the sclerotic foci invade the reflex arcs.

Summing up the symptoms in this case, it is evident that there was enough or more than enough to make the diagnosis of multiple sclerosis, and that there were no symptoms that were incompatible with such a diagnosis. Paoli Pini,[6] reporting cases from Oppenheim's clinic, does not hesitate to make the diagnosis of multiple sclerosis on far less evidence. The literature contains a number of papers devoted to the resemblance of cerebrospinal syphilis to multiple sclerosis, but most of the reported cases are without confirmation by necropsy. B. Sachs[7] pointed out the close resemblance between multiple sclerosis and cerebrospinal syphilis, and remarked that spastic paraplegia of the lower extremities, ocular palsies, optic-nerve atrophy, loss of pupillary reflexes, difficulties of speech, mental changes, apoplectiform seizures, marked remissions in all the symptoms are common to both affections. Nystagmus, intention tremor, and scanning speech are characteristic of multiple sclerosis, and are supposed to be absent in syphilis of the nervous system, but he has seen nystagmus and peculiarities of articulation resembling scanning speech in syphilis. In some cases of syphilis a tremor occurs which differs from the ordinary intention tremor only in that it is persistent and is aggravated on voluntary movements.

Sachs emphasizes the importance of the iridic reflex in making a diagnosis between multiple sclerosis and cerebrospinal syphilis, and considers the complete immobility of one or both pupils strong evidence in favor of syphilis rather than of multiple sclerosis. Indeed, in one of Cassirer's cases of doubtful diagnosis Sachs says that he (Sachs) did not regard the case as one of syphilis because the pupillary reflexes remained normal. In our case of syphilis pupillary rigidity was not present; at first the reflexes were normal; two years later the Argyll-Robertson pupil was observed. Nonne,[8] in his monograph on syphilis of the nervous system, says, in regard to the relation of syphilis to multiple sclerosis, that the latter cannot be mistaken for the former when the clinical picture of multiple sclerosis, as drawn by Charcot, is considered. The course of syphilis of the nervous system is different, and scanning speech, rotatory nystagmus, intention tremor, the general tremor of the trunk and head are not observed in spinal syphilis; this statement can no longer

[5] Amer. Jour. Med. Sci., January, 1903.
[6] Deut. Ztschr. f. Nervenheilk., vol. xxiii, p. 267.
[7] New York Med. Jour., 1891; Phila. Med. Jour., 1898.
[8] Syphilis und Nervensystem, S. Karger, Berlin, 1902, p. 306.

be accepted. If a patient with multiple sclerosis has a history of syphilitic infection the latter proves nothing, and it is probable that syphilis plays no part in the etiology of multiple sclerosis.

Oppenheim[9] thinks that the symptoms of cerebrospinal syphilis may closely resemble those of multiple sclerosis, especially in cases with spastic paraplegia. In both diseases there are cerebral and spinal symptoms, and in each remissions and exacerbations occur. Disturbance of vision, anesthesia, paresthesia, etc., may vary in intensity in each. However, it is rare for the diagnosis to be difficult for a long period, and yet it was difficult in our case for four years. The cerebral symptoms of multiple sclerosis, he says, are very different, viz., nystagmus and scanning speech; and the tremor is almost pathognomonic; stupor does not occur in multiple sclerosis except in the rare apoplectiform attacks, and is almost always observed at some period or other in cerebrospinal syphilis; but it was not present in our patient until a month or two before death. Oppenheim confesses that he has not always been able to decide whether a certain case was one of cerebrospinal syphilis or multiple sclerosis. The partial optic atrophy is the typical form of disease of the optic nerve in multiple sclerosis; when it occurs in syphilis it is usually accompanied by much impairment of sight, whereas an equal degree of atrophy in multiple sclerosis impairs the sight very little. In our patient, in 1903, vision was $\frac{5}{200}$ in the right eye and $\frac{5}{15}$ in the left. Pupillary symptoms are rare in multiple sclerosis.

The spinal symptoms may be very similar in the two diseases. It is strange, he says, that authors have paid so little attention to the differential diagnosis between cerebrospinal syphilis and multiple sclerosis. He refers, however, to the writings of Sachs, Sanger, Gilbert and Lion, Schuster, Uhthoff, Reinhold, Sottas, Marie, v. Bechterew, Cassirer, and Pini, and to these should be added those of Gowers and Krewer.

Some authors hold that syphilis may cause areas of disseminated sclerosis, but does not produce exactly the same symptom-complex as does the true multiple sclerosis. This subject is discussed recently by Guinio Catola.[10] He refers to a case reported by Schuster,[11] in which symptoms of disseminated sclerosis were associated with syphilitic ulceration of the pharynx, indurated glands, and periostitis of the right tibia. All symptoms disappeared under antisyphilitic treatment. This case probably was similar to the one we describe, as one could hardly expect sclerotic areas to disappear under any treatment, and it shows in association with our case that the symptoms of disseminated sclerosis may be caused by the syphilitic infiltration and vascular lesions. The symptoms in Schuster's case were intention tremor of the upper and lower limbs, dragging of

[9] Die syphilitischen Erkrankungen des Gehirns, 1903, 2d ed., p. 5.
[10] Nouvelle Iconographie de la Salpêtrière, July and August, 1906, p. 337.
[11] Berl. klin. Woch., 1885.

the feet, exaggeration of the tendon reflexes, slight contracture of the limbs, and true nystagmus. Catola reports two cases with necropsy which he thinks bear on the question of the syphilitic origin of multiple sclerosis. Muller,[12] in his recent book on multiple sclerosis, refers to the resemblance this disease may have to cerebrospinal syphilis, but draws his conclusions from the literature rather than from personal experience.

The difficulties in the diagnosis have been regarded as the cause of the apparent comparative rarity of multiple sclerosis in America. It may be that many cases, especially those of the *formes frustes*, are overlooked by superficial examination, but, on the other hand, there seems at present a danger that much will be called multiple sclerosis that in reality is some other disease.

RECURRENT FACIAL PALSY, WITH REFERENCE TO CERTAIN ETIOLOGICAL FACTORS.

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Oppenheim classes facial palsy as "the most common neural paralysis." Charles K. Mills speaks of it as "one of the most frequent and therefore one of the most important forms of paralysis." Allen Starr gives 7 per cent. as the number of facial palsies that recur on the same or the opposite side. Wm. G. Spiller believes this to be a fair estimate. I wish to present the records of two cases of the recurrent type that were treated at the Dispensary for Nervous and Mental Diseases of the Polyclinic Hospital, and I take this opportunity to thank Dr. Spiller for his permission to report them. In addition to the records of these two cases I shall briefly discuss an underlying cause predisposing to facial palsy in general that, I believe, has not been emphasized sufficiently.

Case I.—Jacob S., a tailor, aged forty-six years, was born in Russia. Both of his parents were over sixty years of age when they died. One brother died of tuberculosis. Four brothers and one sister are alive and apparently healthy. He denies venereal disease and says he has always been healthy. There are three other items of importance in his history: (*a*) He has been for years an habitual user of alcoholics in moderation and cigarettes in great excess; (*b*) he eats a great deal of meat; (*c*) he has had a number of attacks of painful throat that were not inflammatory in character—they were rheumatic attacks, to judge from his description of them. He came to the

[12] Die multiple Sklerose des Gehirns und Rückenmarks, p. 250.

Polyclinic Hospital October 21, 1904, complaining of left-sided facial palsy associated with pain in the same side. The aural examination was made by Dr. Packard, who reported a normal condition. The notes read: "He cannot move, on the affected side, the muscles of his forehead, face, or mouth. The mouth is drawn to the right on innervation. The nasolabial fold is absent on the left side and the left eye cannot be closed. He can bite equally well on both sides and his tongue is protruded in the median line. The reactions to the faradic and galvanic current are normal."

Ten days later his general condition was as before, but the electric reactions were lost. Eventually this case resulted in a cure. It was a typical case of the classical type, without any special cause assigned to it.

On June 12, 1905, while riding in a train he felt a recurrence of the symptoms of palsy on the *right* side of his face; it soon became complete as before. He is positive that the window next him was not open and asserts that three days before this (June 9) he had felt decided pain behind the right ear. The duration of this second attack was shorter and the course less severe than the first, and on the tenth day the notes report a prompt reaction to electric stimulation of nerve and muscle.

CASE II.—Jacob K. is four years old and was born in Philadelphia. His parents are alive and generally well; his mother complains a good deal of rheumatic pains in her muscles. There are six children in the family. One child, aged thirteen years, has, according to the mother, disease of the kidneys; the rest, including the patient, have always been considered healthy. His mother says the patient had an attack similar to the present one two years ago. The history of the second attack is that he woke on the morning of June 3, 1905, with the symptoms of left-sided facial palsy—the same side that was affected by the first attack. He had been sleeping in a draught during the night of onset. There was no pain or tenderness associated with this attack. Physical examination showed complete paralysis of the left side of the face, somewhat exaggerated knee-jerks and normal electric reactions over the affected area. Sixteen days after this the functions of the affected side were to all appearance normal and the reaction of nerve and muscle equal on both sides excepting the lips.

Various etiological factors have been advanced to explain this "commonest neural paralysis."

Oppenheim asserts: "There is no doubt that exposure to cold (draughts, sleeping beside an open window, etc.) is the cause of 70 per cent. of the cases in otherwise normal individuals." And, as a matter of fact, these are the cases that are seen so often in the nervous dispensaries—patients who are otherwise normal, apparently. Their histories do, in the great majority of cases, include an exposure to cold as the given cause of the attack; and yet to all appearances

they are perfectly normal individuals and luck the special causes that would explain the attack, such as petro al di case, suppurative conditions in the region of the facial nerve, etc. Indeed, they often seem to lack any sufficient cause or sum of causes that would account for their condition. The natural query is, Why, then, should these people be subjected to this alarming set of symptoms?

Answers to this have been many and varied. Of those who see a great many of these cases, a number believe that in very many of them the predisposing cause is a congenital or acquired narrowing of the bony canal through which the facial nerve makes its way. This could certainly explain why a number of these otherwise normal people, given some exciting cause, would be liable to this form of paralysis. But in so few cases can this be demonstrated that, while it explains the liability, it is not altogether satisfactory as regards the first cause.

There is one simple cause that I believe has not been emphasized sufficiently, and that is a defective condition of the intestinal tract associated with a faulty elimination of waste products by way of the kidneys, the lowered tone of the nerve being a secondary and consequent symptom.

We know the class of persons (both overfed and underfed) who complain of neuralgias, rheumatic pains, gouty affections, etc. Some of them are distinctly neuropathic, others are not and yet they are subject to the same ailments, and so many of them present themselves suffering from the alarm caused by a facial palsy and can give no satisfactory cause. In attempting to find an explanation for their attacks my attention was forcibly drawn to the fact that most of those I saw presented a coated tongue, told of former headaches or neuralgias, or complained of rheumatism or attacks of rheumatic sore throat. As to sore throat Dr. Grayson asserts that 9 out of 10 cases of sore throat, tonsillitis, and painful throat originate in gastro-intestinal disorder and are allied to gout. We know how often the common neuralgic pains and rheumatic pains are relieved together with the relief of the liver and bowels; and how many are helped when we have discovered that the urine passed in twenty-four hours amounts to a good deal less than the normal and correct this condition of faulty elimination.

The medicinal treatment has been to a certain extent empirical, but is the same as we prescribe for rheumatism, gouty affections, sore throat, and the like. It is well known that the salicylates are exhibited with good results in these cases of facial palsy. The same remedy associated with catharsis is indicated in the other list. Brunton asserts that the salicylates are carried as such in the blood and their antiseptic qualities are well known, and he recommends them together with the bromides in gouty and lithemic cases for their nervous irritability. He further asserts in this connection that "no other drug causes such a flow of bile."

There appears to be a true basis for the belief that these varying ailments are in some way closely connected.

I believe that these cases of facial palsy are associated with the diseases that are brought about by a storing up in the body of the toxins or poisons normally thrown off by the bowel, skin, and kidneys, and that they are due to a constant or repeated poisoning of the nerves by a circulation that is vitiated by this unhygienic state of affairs. The exciting cause may be exposure, traumatism, or an added intoxication, and yet the result is due to the underlying condition of the nerves themselves, which in turn is due to the faulty elimination.

Applying this to the two cases in hand as being typical facial palsies, we recollect that Case I—the man—is a tailor (an occupation notorious for gastro-intestinal disorders), who imbibed alcoholics regularly, ate meat in excess, and used tobacco to excess. He had a thick. coated tongue and an offensive breath. His history showed repeated attacks of sore throat and he had frequent headaches.

In such a man, saturated with the intoxication from three sources and given, let us say, a nerve constricted and engorged and situated in the most exposed part of the body; now let that man ride in a draughty car in summer, thus aiding the rapid evaporation of the perspiration that would naturally flow excessively, and there is an ideal situation for the onset of a facial palsy.

In Case II we have a boy of a neuropathic habit, another one like Case I, of that class of people that are so wrongly fed and hard worked—the Russian Jews—and showing, besides the paralysis, no other symptoms than a coated tongue, lack of nourishment due to gastro-intestinal inaptitude, and having a mother afflicted with neuralgias most of the time. The parents of the boy were well-fed individuals and said they tried to overfeed the boy, hoping to fatten him.

Both of these cases can better be explained by the lack of proper alimentary hygiene than in any other way. Of course the direct or exciting cause is often as in Case II, exposure to draughts and cold while the natural body resistance is lowered—as during sleep or in the summer or when the perspiration is too quickly evaporated over exposed skin surfaces, etc.—but most often the underlying cause is, I believe, disordered hygiene of the alimentary tract and the consequent failure to eliminate waste products through the natural avenues. The good effect of eliminative and antiseptic treatment, with proper hygiene of the alimentary tract, supports this belief.

THE BACTERIOLOGY OF THE BLOOD IN TYPHOID FEVER.

AN ANALYSIS OF 1602 CASES.[1]

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During the last six years we have made bacteriological examinations of the blood in 123 cases of typhoid fever in the wards of the Second Medical Division of Bellevue Hospital. In 1904 we published an analysis of 604 cases of typhoid fever (for the most part collected from the literature) in which the blood had been examined bacteriologically. Seventy-five per cent. of these cases, examined at all stages of the disease, showed the presence of the typhoid bacillus. Bacteriological examinations of the blood of typhoid and suspected cases have been made routine practice in many hospitals, and the number of cases reported to date, including our own, reaches a total of 1602. The present analysis includes all the cases in our former paper, except the reports of individual cases.

Methods. We usually draw 10 c.c. of blood into an all-glass syringe from a vein at the bend of the elbow. In our earlier experiments (1901 to 1903) we used broth flasks, putting 2 to 3 c.c. of blood into each 100 c.c. of broth. Later, on learning that Busquet and other French authors had had extraordinary success by using very large quantities of broth, we followed their method of diluting each cubic centimeter of blood in about 200 c.c. of broth, but the results were not appreciably better than before. Since August, 1906, however, we have had very marked success with ox-bile, as recommended by Conradi. Ox-bile not only prevents coagulation, but inhibits the bactericidal action of drawn blood and affords an excellent culture medium for typhoid bacilli. Our tests on this point have fully confirmed the previous observations of Conradi, Kayser, and others.

The method followed has been to take ox-bile 90 c.c., glycerin 10 c.c., and peptone 2 grams. The mixture is distributed into small flasks, 20 c.c. in each, and sterilized. Three of these flasks are used for each examination, about 3 c.c. of blood being run into each. The flasks are then incubated, and the next morning streaks are made from each flask over the surface of a litmus-lactose-agar plate. If microörganisms are present, a growth may be observed in five or six hours. If the growth does not redden the medium and is found

[1] Read at a meeting of the New York Academy of Medicine, March 7, 1907.

to be a bacillus resembling the typhoid organism, it is tested for the Widal reaction with immune serum. By this procedure we are often able to determine if the case is one of typhoid fever or not within twenty-four hours after drawing the blood.

We give below a table of the cases included in this report:

TABLE OF REPORTED CASES.

Number.	Authors.	Number of cases.	Bacillus found.	Bacillus not found.
1	Ruediger	32	20	12
2	Fox	14	1	13
3	Cole	15	11	4
4	Hewlett	25	21	4
5	Widal	25	17	8
6	Busquet	83	83	0
7	Courmont and Lesieur	37	37	0
8	Schottmueller	119	98	21
9	Kerr and Harris	56	31	25
10	Castellani	14	11	3
11	Auerbach and Unger	10	7	3
12	Kuehnau	21	9	12
13	Warfield	48	33	15
14	Janesco	19	8	11
15	Rolly	50	43	7
16	Berri	13	7	6
17	Duffy	88	62	26
18	Hirsh	97	75	12
19	Memmi	30	18	12
20	Richard	50	44	6
21	Perquis	40	38	2
22	Fornet	19	14	5
23	Jochmann	30	25	5
24	Harrison	8	5	3
25	Eppenstein and Korte	6	5	1
26	Rusta	12	12	0
27	Korte and Sternberg	22	22	0
28	Trappe	38	25	13
29	Brion and Kayser	233	153	80
30	Kayser	75	50	25
31	Loiseleur	65	63	2
32	Epstein	85	68	17
33	Coleman and Buxton	123	81	42
		1602	1197	405

The table shows that of the total of 1602 cases, 1197 (or 75 per cent.) gave a positive result. The examinations were made at all stages of the disease and by different methods. Since in our experience the bile method[2] is the only one which may confidently be depended upon, such a large percentage of positive results goes far to prove that the bacillus is present in the blood in practically all cases of typhoid fever.

ANALYSIS OF THE CASES BY WEEKS. The day of the disease upon which the examination was made is mentioned in 1137 cases only. To be more exact, this represents the number of examinations, not of cases, for in many instances more than one examination was made in a case.

First Week. Of 224 examinations in the first week of the disease, 200 (89 per cent.) were positive. The earliest positive result has

[2] We have not tried the glucose method of Epstein.

been reported by Widal, who recovered the bacillus from the blood on the second day of the disease. The reported positive results become more frequent as the end of the first week is approached, only, we believe, because the disease is not suspected earlier and the examinations made, or because the cases do not come under observation.

Second Week. Of 481 examinations made in the second week of the disease, 351 (73 per cent.) were positive.

Third Week. Of 208 examinations made in the third week of the disease, 178 (80 per cent.) were positive.

Fourth Week. Of 103 examinations made in the fourth week of the disease, 90 (88 per cent.) were positive.

After the Fourth Week. Of 58 examinations made after the fourth week of the disease, exclusive of relapses, 15 (26 per cent.) were positive.

Very few statements are made concerning the clinical histories of the cases in and after the fourth week, though some of them are reported as severe and of long duration. As in our first analysis, the percentage of positive results is greatest in the first week and steadily declines thereafter.

We have already called attention to the remarkably successful results of Bunquet and others, who recovered the bacillus from the blood in approximately 100 per cent. of their cases. Our results since the adoption of the bile method have been equally successful, standing out in marked contrast to those with broth. In all we have used this method in 31 cases. As a rule, the blood was examined as soon as a case of fever without obvious cause entered the hospital, and before the diagnosis was established. Six of these 31 cases were diagnosticated ultimately as certainly not typhoid fever; 3 of the cases pursued the clinical course of typhoid fever, but gave neither a positive blood culture nor a positive serum reaction against any member of the typhoid-colon group. In fact, after examinations of urine, feces, opsonic index, and injections of tuberculin, a satisfactory diagnosis could not be made. It seems only fair to exclude these cases. One case ran an eleven-day temperature, the maximum being 101°, but for the most part ranging between 99° and 100°. The first blood culture was taken on the eighth day. There was a difference of opinion as to the diagnosis. The patient had an old tuberculous process at one apex. This case likewise may be fairly excluded. We made three examinations of his blood.

The remaining 24 cases were typhoid fever clinically and by serum reaction and all gave positive bacteriological results. The examinations were made from the fifth to the twenty-first day in a long-duration case.

The various series of cases in the table giving approximately 100 per cent. of positive bacteriological results are too numerous to be

accidental. They compel the conclusion that the typhoid bacillus is present in the blood in every case of typhoid fever and that failure to recover it is due to error of technique. The diminishing percentages of the larger analysis in the later weeks of the disease do not indicate, then, that the bacillus has disappeared from the blood in the negative cases, but point rather to diminishing numbers of bacilli, whose presence imperfect methods have failed to reveal. All investigators except Conradi are agreed that the bacillus disappears from the blood at or about the time the temperature falls to normal. Conradi claims that the bacillemia persists into convalescence. We have repeatedly examined the blood in the last day or two of the febrile period and not once have we recovered the bacillus. Therefore, it seems probable that the typhoid bacillus is not only present in the blood in every case of typhoid fever, but that it is present throughout the course of the disease, or at least to within a day or two of complete defervescence.

THE SIGNIFICANCE OF THE BACILLEMIA. If future observations confirm the conclusion that the typhoid bacillus is present in the blood of every case of typhoid fever throughout its course, the current conception of the pathogenesis of the disease should be modified. Typhoid fever can no longer be regarded simply as an infection of the body with typhoid and related bacilli (Bacillus paratyphosus, etc.). The typhoid bacillus may be present in the body and actively growing, yet the patient not have typhoid fever. It has been shown, for example, that the bacillus may live and multiply in the intestine of healthy persons. The patient is infested and a menace to others, but is not infected. The number of cases of biliary infection with the typhoid bacillus, without a previous or existent typhoid fever, is fairly large and is increasing. At least two cases of cystitis, caused by the typhoid bacillus in persons without a history of typhoid fever, have been recorded. (There is little probability, however, of the absorption of endotoxins in any quantity in cholecystitis and cystitis). In the post-typhoid bone and other inflammatory lesions the lodgement and growth of the bacillus do not produce the characteristic symptoms of typhoid fever, in spite of the fact that large amounts of endotoxin should be liberated and absorbed when the abscesses are multiple. The very term used to describe these conditions, "post-typhoid," indicates that the typhoid fever *per se* has subsided. The temperature curve conforms to the so-called septic type.

Therefore, it seems that to produce typhoid fever the bacillus must not only be present in the body and growing, but that it should grow in a situation whence it has free access to the blood. In our first paper we expressed the opinion that in typhoid fever the earliest and principal seat of infection is the blood, and that the disease should be regarded as a bacillemia. From the work done by one of us on the absorption of the typhoid bacillus from the peritoneum,

and from the fact that in typhoid fever the lymph nodes and spleen contain such enormous numbers of bacilli, we are disposed to modify this view and to conclude that in typhoid fever the bacillus first finds its way from the alimentary tract to the lymphopoietic system, including the spleen, where it develops chiefly and from which it invades the blood stream. We think it doubtful whether the bacillus multiplies in the blood, but rather that its presence there represents simply an overflow from the lymph organs. Under this interpretation the presence of the bacillus in the blood does not constitute a true septicemia.

The absorption experiments above referred to also indicate that destruction of the typhoid bacilli proceeds most rapidly in the blood. This observation, together with the fact that the bacillemia persists throughout the disease, suggests the following view of the pathogenesis of typhoid fever: That the disease is caused by the destruction of vast numbers of bacilli in the blood, with the liberation of their endotoxins, and the consequent reaction on the part of the host. When the endotoxins are liberated elsewhere in the body, *e. g.*, in abscesses, the symptomatology is not that of typhoid fever.

This conception of the nature of typhoid fever is borne out by analogy. It is known that Bacillus paratyphosus may infect the intestine and produce the clinical picture of gastro-enteritis, but that when it invades the lymph organs and blood it produces a disease clinically indistinguishable from typhoid fever. Diplococcus lanceolatus and the various streptococci furnish similar analogies in that they produce different affections according to the regions they attack.

There is another matter to which we would call attention in this connection. The idea still prevails in some quarters that the course of typhoid fever may be influenced and even shortened by the use of intestinal antiseptics. Such opinion is based on an erroneous conception of the nature of typhoid fever. After invasion of the body proper by the bacillus the battle-ground shifts from the intestines to the blood, and the employment of intestinal antiseptics with the idea of controlling the disease is, to say the least, irrational.

THE RELATION OF THE BACILLEMIA TO THE COURSE AND TYPES OF THE DISEASE. *Course.* The analysis of the cases in the various weeks of the disease suggests the following relation of the bacillemia to the course of typhoid fever: In the earlier stages the bacillus invades the blood in greatest numbers. Later, as the disease is approaching a favorable termination, the diminution in the number of bacilli in the blood is simply an index of less active development in the lymphatics and spleen. If the disease in any case pursues a long-duration course, that beyond the usual three weeks, the bacillus may be recovered from the blood as long as the temperature persists. We have isolated the bacillus late in such cases repeatedly. There appears then to be a definite relation in the evolution of typhoid fever between the symptoms and the bacillemia. The

increasing intensity of the symptoms in the earlier period of the disease corresponds to active growth of the bacilli. They invade the blood stream in increasing numbers and are there destroyed. Then comes the stationary period, when the ratios of growth and destruction appear uniform. The steep-curve period corresponds to a diminishing bacillemia, and defervescence to the complete disappearance of bacilli from the blood. In other words, the duration of the febrile movement is measured by the persistence of the bacillemia. As already stated, Conradi is the only investigator who claims that the bacillemia continues into convalescence.

Ewing has expressed the opinion that "the degenerative changes in the liver, kidneys, and lymphoid organs, while initiated by the bacterial proteids, possess certain self-perpetuating tendencies," and therefore "typhoid fever is a combination of a specific bacterial intoxication and a somewhat peculiar auto-intoxication, the former element being more prominent early, the other later in the disease, but both developing simultaneously." We are unable to accept this conception of the pathogenesis of typhoid fever. It appears inconsistent with the facts developed by our studies. We maintain that exclusive of convalescence, which should be regarded as the period of repair, degenerative changes occur only in the presence of active growth and destruction of bacilli. We have shown that convalescence is established immediately upon the disappearance of the bacilli from the blood, and there are reasons to believe that it is not interrupted except as the result of a fresh growth of bacilli. While the bacilli disappear from the blood at or just before defervescence, it is improbable that all the bacilli in the body have been destroyed. Otherwise, relapses and post-typhoid inflammatory lesions would be impossible. Unless then it can be shown that the symptoms of typhoid fever would persist after the complete destruction of all bacilli in the body, we think that Ewing's position is untenable.

Types. The bacillemia apparently bears no relation to the type or severity of the disease except in so far as regards numbers of bacilli. The bacillus is found in the blood equally, but not with the same persistence, in the mild as in the severe cases, and in the cases of short as well as of long duration. We have found the bacillus, for example, in cases lasting ten, thirteen, and fourteen days, and on the twenty-seventh day of a long-duration case. The importance of the definite establishment of the nature of these short-duration cases can scarcely be overestimated from the epidemiological standpoint. The serum reaction has done much to clear up their diagnosis, but the final proof has remained for the bacteriological examination of the blood. We make only a brief reference to these cases here, as we shall deal with them at length in the near future.

Relapses. The blood has been examined bacteriologically by various investigators in 33 relapses. The typhoid bacillus has been

recovered in 30 (90 per cent.) of the cases. We suggested in 1904 that a relapse in typhoid fever is due to reinvasion of the blood by the bacillus. Reinvasion of the blood with destruction of the bacilli probably cause the symptoms of a relapse, but the underlying conditions which inaugurate active development of the bacilli after their growth has once been brought under control are unknown. We feel safe in asserting that a relapse is not due to reinfection with the typhoid bacillus from the intestine as the result of intestinal trauma brought about by dietary irregularities. We do not wish to intimate, however, that we believe the occurrence of a relapse is entirely independent of diet or to be understood as advocating a liberal diet in typhoid fever. We are not prepared as yet to express an opinion upon this subject.

THE RELATION OF THE BACILLEMIA TO THE SERUM REACTION. In our former paper we stated that it would seem likely on *a priori* grounds that the typhoid bacillus is always present in the blood before the serum reaction develops, for the reason that endotoxins should be liberated before the agglutinins could be formed. The following table clearly illustrates the truth of this conclusion:

TABLE SHOWING RELATION OF BACILLEMIA TO SERUM REACTION.

Author.	Number of cases.	Bacillus found and Widal reaction negative.
Hirsh	100	23
Jochmann	20	5
Rolly	50	16
Duffy	88	18
Buxton and Coleman	123	32
	391	94

Of the 55 cases of Hirsh and ourselves, which showed the presence of the bacillus in the blood before the serum reaction could be obtained, 23 were in the first week, 26 in the second, and 6 in the third. The diagnostic value of these results in cases in which only one, or a few, serum tests have been made is important. A negative serum reaction may have no significance even in the third week of the disease. Moreover, Dr. Hastings has shown in some of our cases, especially those of short duration, that a positive serum reaction may be present for only two or three days. If the serum reaction had not been tested on those days, the result would have been recorded as negative throughout the disease. For the complete diagnosis of an obscure case by the serum reaction the tests should be made daily.

CONCLUSIONS. 1. The typhoid bacillus is present in the blood of every case of typhoid fever throughout its course.

2. The bacillemia in typhoid fever does not constitute a true septicemia, but it represents an overflow of bacilli from the lymphopoietic organs.

3. The clinical picture of typhoid fever results only from infection of the lymphopoietic organs by the typhoid bacillus, with invasion of the blood stream and destruction there of vast numbers of bacilli.

4. The endotoxins of the typhoid bacillus are not cumulative in action and convalescence from the typhoid fever *per se* is established within a few days after the disappearance of the bacilli from the blood.

We wish to express our thanks to Profs. Loomis, Thompson, and Dana for the privilege of studying the cases.

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INFLUENCE OF IODINE PREPARATIONS ON THE VASCULAR LESIONS PRODUCED BY ADRENALIN.

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About two years ago L. Loeb and T. G. Githens[1] instituted a series of experiments to determine the experimental conditions in which adrenalin injections into rabbits would cause arterial changes.

[1] The Effect of Experimental Conditions on the Vascular Lesions Produced by Adrenalin, Amer. Jour. Med. Sci., 1905.

The results obtained were as follows: (1) Pyrocatechin, even though injected in doses sufficiently large to produce convulsions and continued over a long period, produces no, or only trifling, changes in the bloodvessels, this in spite of the facts that pyrocatechin raises the blood pressure and that adrenalin and pyrocatechin bear to one another a distinct chemical relationship. It seems, therefore, that adrenalin does not act, or does not alone act, through its power of raising blood pressure in the production of the changes in the vessel walls. (2) Previous thyroidectomy does not hinder the action of adrenalin on the vessel walls, a conclusion contrary to that of Lortat-Jacob and Sabarianu, who have reported such an action. (3) The usual vascular changes do not seem to be influenced by simultaneous administration of potassium chromate and adrenalin, or by tying a ureter and then administering adrenalin, although potassium chromate was given in doses sufficiently large to cause albuminuria, during the whole course of the experiment. Thus the vascular lesions produced by adrenalin do not seem to be increased or decreased by experimental lesions of the kidney. (4) If pregnant animals were injected with adrenalin from the beginning of pregnancy the pregnancy followed its normal course, as did the labor; the aortas of the newborn showed no lesions, while those of the mothers showed less tendency toward change than did aortas of non-pregnant animals; at least the conclusion may be drawn that pregnancy does not predispose toward vascular changes. (5) The number of the injections, and the quantity used at each injection of adrenalin are of far less importance than is the length of time between the commencement of the injection and the death of the animal; this does not set aside the vascular changes which can be found after a short period, for several such cases were found. (6) Histologically there was primarily found a necrosis of the musculature of the media, the elastica being at first preserved. After this there follows a calcification, stretching of the elastica lamellæ, and then a splitting up and disappearance of the elastic membranes. These conclusions were supported by experiments on forty rabbits.

In their communication Loeb and Githens stated that this experimental method of producing lesions in bloodvessels will provide us with means of determining accurately the effect of certain substances believed to be curative of arteriosclerosis in man. Although there exists a marked difference between the histological characters of arteriosclerosis in man and the microscopic lesions produced by adrenalin injections, it is nevertheless not yet certain how fundamental these differences are and to what extent they may be determined by a special kind of response of the species used in the experiment; but even conceded that this difference between arteriosclerosis and changes produced by adrenalin is a decisive one, there exists in man a certain lesion of the bloodvessels of the extremities seen in old age in which the media alone is affected and in which marked

calcification of this coat is found. Soon after the vascular changes produced in rabbits by the injection of adrenalin had been discovered, attention was drawn by some pathologists to the similarity between these vascular lesions in the extremities of old persons and the lesions produced by adrenalin. A certain similarity exists also between syphilitic aortitis and the lesions produced by adrenalin, as far as the localization of the lesions is concerned.

It is, therefore, not altogether without interest to test the effect of certain chemical substances on the vascular lesions in rabbits; under such experimental conditions we are able to determine, with much greater accuracy, the efficacy of these drugs, since we are able, at the same time, to conduct the necessary control experiments which we are rarely, or never, able to do in treating vascular lesions in man.

One of the first substances which suggested itself for experimentation was potassium iodide,[2] which lowers the viscosity of the blood and may in this way influence the circulation, counteracting the effect of the increased blood pressure and thus preventing changes of arterial walls. Shortly before we undertook these experiments a brief communication of v. Korangi[3] appeared in which he stated that by simultaneous injection of iodipin and adrenalin it was possible, almost entirely, to prevent the effects of adrenalin on the bloodvessels. Boveri[4] found a beneficial effect of iodipin in a few cases. Cummins and Stout[5] observed that in two rabbits simultaneously injected with adrenalin and potassium iodide, no vascular lesions were present after the death of the animal.

Quite recently, after our experiments had been almost concluded, there appeared a paper by J. Biland,[6] in which, in experiments carried on simultaneously and independently of those of Korangi, he came to the conclusion that potassium iodide far from having a beneficial effect, aggravated the lesions produced by adrenalin. Under these conditions it might not be without interest to give the results of our investigations, especially as they are based on a much larger number of experiments than those carried out by any of the aforementioned investigators.

In the first place we made (1) a comparative investigation of different iodine preparations, using iodipin as well as potassium iodide; (2) we applied the latter in some cases subcutaneously, in some cases intravenously, in order to determine whether the mode of application was of importance; (3) we used the various substances in different doses, using in some animals very large, in others

[2] The use of this substance had already been planned by Loeb and Githens in connection with their former experiments.

[3] Ueber die Wirkung des Iods auf die durch Adrenalin erzeugte Arterionekrose, Deutsch. med. Woch., April 26, 1906, pp. 679, 680.

[4] Deutsch. med. Woch., 1906, Nr. 22.

[5] University of Penna. Med. Bull., July, 1906.

[6] Deutsch. Arch. klin. Med., August 28, 1906.

very small doses; (4) we tested another substance, bromipin, in order to determine whether or not a possible effect of iodine preparations was a specific one; and (5) we included in our experiments the action of potassium sulphocyanide, because Pauli had suggested, from conclusions based on theoretical reasons, that potassium sulphocyanide might be able to take the place of potassium iodide in its therapeutic application and might even be more efficient than the iodine preparation.

Three series of experiments were carried out in the course of our work and the results are seen in the abstracts of our protocols.

In summarizing these results we shall divide each set into two classes: (1) Those animals which received but a few injections,

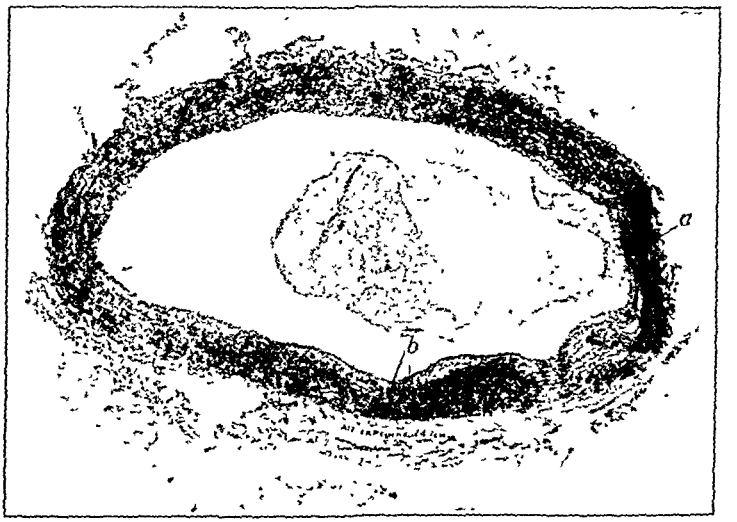

FIG. 1.—Section through one of the large vessels branching off from the arch of the aorta. In this case the aorta itself was normal macroscopically, although the smaller vessel shows calcareous plates (*a* and *b*). The rabbit had received 23 injections of adrenalin and iodipin (3.4 c.c adrenalin, 46 c.c. iodipin). It lived from July 8, 1906, until it was killed on August 22, 1906.

and (2) those which received a comparatively large number of injections; we place those which received more than ten injections in the latter class, and all which died or were killed before receiving this number in the former class. In speaking of the changes in the aorta we will use four terms: *normal; changed* when there is unevenness but no true macroscopic calcification; *slightly calcified* when there are but few small plaques well scattered or only in one small locality; and *markedly calcified* when the calcareous plaques are large and cover a considerable portion of the vessel wall.

We find the results to be as follows:

SERIES I. *Set A (control)*: Injected every other day; adrenalin 0.1, 0.15, 0.2 c.c. Short-lived: 3 rabbits, of which 2 showed normal

aortas and 1 slight calcification. Long-lived: 8 rabbits, of which 1 was normal, 4 showed slight calcification of the aortas, and 3 showed marked calcification.

Set B (Iodipin and Adrenalin): Injected every other day; iodipin 2 c.c., adrenalin as in Set A. Long-lived: 4 rabbits; 1 presented a normal aorta, 2 were slightly calcified, and 1 showed marked calcification in the vessels. It may be worth noting the fact that in this series none of the rabbits died before the tenth injection.

Set C (KCNS and Adrenalin): Injected every other day; KCNS 0.1 c.c. of 5 per cent. solution, adrenalin as in Set A. Subcutaneously; short-lived: 3 rabbits; 2 showed a normal aorta, 1 showed a changed aorta. Long-lived: 2 rabbits; 1 showed the aorta normal, 1 showed slight calcification. Intravenously; short-lived: 2 rabbits; 1 showed a normal aorta, and the other showed marked

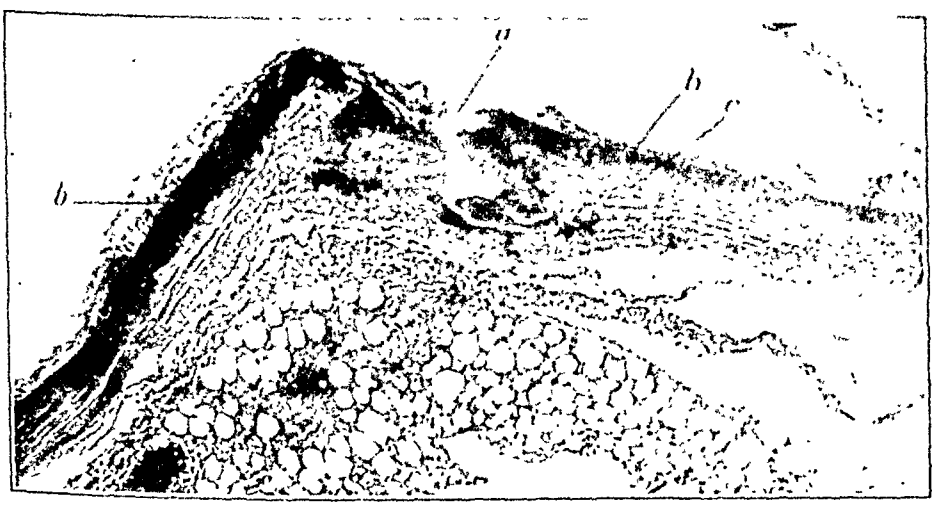

FIG. 2.—Section through the upper part of the descending aorta of the rabbit which had received 6 injections of adrenalin (0.8 c.c.), iodipin (18 c.c.), and KI (1.0 gram) in the course of twelve days. The aorta was much changed, showing calcification (*b*), necrosis, and distention (edema?) of the media (*c*), and a partial rupture of the wall of the aorta (*a*).

calcification. Long-lived: 4 rabbits; 1 showed a normal aorta, 1 showed the aorta changed, 2 showed slight calcification. Those rabbits which received the KCNS subcutaneously died earlier and tended more toward diarrhœa than those receiving the injection intravenously. In this set KCNS was given in larger doses than in any of our later series.

Set D (Bromipin and Adrenalin): Injected every other day; bromipin 2 c.c., adrenalin as in Set *A*. Short-lived: 10 rabbits; 4 showed a normal aorta, 4 showed simply a changed condition, and 2 had the aorta markedly calcified. Of the 4 which showed normal aortas, 3 died very early—before they had received more than four injections. Long-lived: 2 rabbits, both of which showed the aorta markedly calcified.

SERIES II. *Set II (control)*: Injected every day; adrenalin, 0.1, 0.2, 0.25, 0.3, 0.35, c.c. Short-lived: 1 rabbit which showed a normal aorta. Long-lived: 1 rabbit which showed a normal aorta.

Set E[1] *(Iodipin and Adrenalin)*: Injected every other day; iodipin starting with 4 c.c. and running up the dose until 9 c.c. was given at each injection; adrenalin as in Set *H*. Short-lived: 3 rabbits; 1 showed changes in the aorta, 2 were markedly calcified. Long-lived: 3 rabbits; all 3 showed fairly marked calcification. In this set iodipin was given in the largest-sized doses used during the experiments.

Set E[2] *(Iodipin, KI. and Adrenalin)*: Injected every other day; iodipin, 3 c.c.; KI 0.1, 0.15, 0.2 gram; adrenalin as in Set *H*. Short-lived: 6 rabbits; 1 showed the aorta changed, 2 showed slight

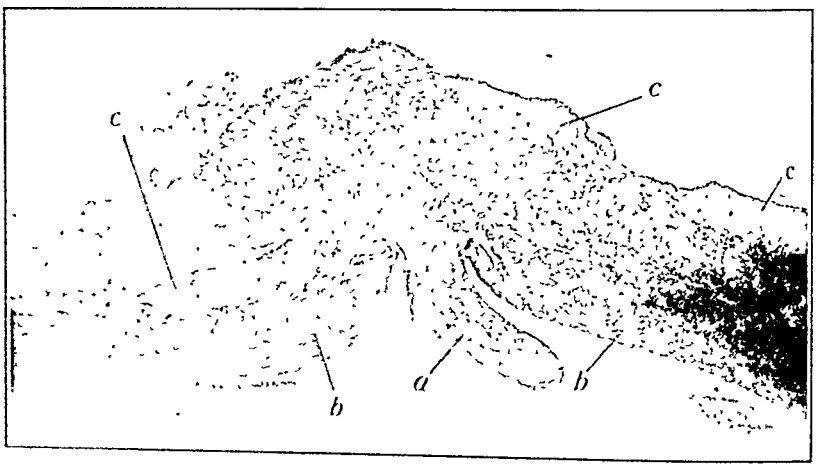

FIG. 3.—Section through the upper part of the descending aorta. The media of the vessel wall is entirely necrotic (*b*). The vessel had ruptured and a thrombus (*a*) formed. The extravasated blood (*c*) is found in the adventitia of the aorta. The rabbit had received 18 injections of adrenalin (2.1 c.c.) and iodipin (36 c.c.). It lived from July 8, 1906, until it was killed, August 11, 1906. The aorta was much changed.

calcification in the aorta, 3 showed the aorta markedly calcified. It is peculiar that all the animals of this series died shortly after the injections were started, none receiving more than seven injections, nor living more than fourteen days after the injections were begun. We noticed at the site of the KI injection (which was given subcutaneously) a hardening and blackening of the skin which gave the appearance of a charred piece of flesh; this condition was preceded by an intense inflammation which passed on to this blackened condition. There can be little doubt that the KI called forth this change.

Set G (KCNS and Adrenalin): Injected every other day; KCNS 0.025 c.c. (5 per cent. solution), adrenalin, as in Set *H*. Short-lived: 3 rabbits; all of which presented normal aortas. Long-

lived: 3 rabbits; none showed any change in the aorta. In this set KCNS was given intravenously, as we believed from our results in our first series that it acted to better effect when administered in this fashion. Medium-sized doses of KCNS were used in this series.

Set F (*Bromipin and Adrenalin*): Injected every other day; bromipin, 0.5 c.c., adrenalin as in Set *H*. Short-lived: 3 rabbits; 1 showed a normal aorta, 2 showed the aorta markedly calcified. Long-lived: 3 rabbits; 1 showed a normal aorta, 1 showed slight calcification, and 1 showed marked calcification of the aorta.

SERIES III. *Set D* (*control*): Injected at first every other day, later every day; adrenalin, 0.1, 0.2, 0.3 c.c. Short-lived: 2 rabbits; 1 showed a normal aorta, 1 showed a slight change. Long-lived: 3 rabbits; 1 had a normal aorta, 1 showed changes, and 1 showed marked calcification. Here, as in the other control sets, we note the uncertainty of the action of adrenalin in producing vascular lesions.

Set A (*Iodipin and Adrenalin*): Injected at first every other day, later every day. Iodipin, 2 c.c.; adrenalin, as in Set *D*. Short-lived: 4 rabbits; 1 showed the aorta changed, 3 showed marked calcification.

Set C (*KCNS and Adrenalin*): Injected at first every other day, later every day; KCNS 0.012, 0.01 c.c. of (5 per cent. solution) adrenalin as in Set *D*. Short-lived: 2 rabbits; 1 showed the aorta normal, 1 presented marked calcification. Long-lived: 8 rabbits; 3 presented a normal aorta, 2 showed the aorta changed, 2 had slight and 1 marked calcification. KCNS, which was injected intravenously, was here used in the smallest doses given during the course of the experiments; the smallness of the dose may perhaps account for the increased effect of the adrenalin as compared with Set *G*, Series II.

Set B (*KI and Adrenalin*): Injected at first every other day, later every day; KI 0.015, 0.05, 0.058, 0.08 gram; adrenalin as in Set *D*. Short-lived: 1 rabbit, showing slight calcification in the aorta. Long-lived: 5 rabbits; 2 showed the aorta only changed, 1 showed slight calcification, and 2 showed marked calcification. KI was administered intravenously and in considerably smaller doses than in Set E^2, Series II.

We may summarize the results of these series as follows: of the 18 rabbits used in the control sets, 7 showed no changes in the aorta, 2 showed changes in the vascular walls, 4 showed slight calcification, and 4 showed marked calcification.

Of the 15 rabbits of the iodipin sets, only 2 showed normal aortas, 2 showed changes in the vessel, 2 showed slight, and 9 marked calcification of the vessel.

Of 18 rabbits injected with bromipin, there were 6 with normal aortas, 4 showed changes of the vessel walls, 2 showed slight calcification, and 7 showed marked calcification of the aorta.

Of 6 rabbits treated simultaneously with iodipin and KI none

escaped the effects of the adrenalin; the aorta was changed in 1 case, 2 showed slight calcification, and 3 showed marked calcification.

Of 6 rabbits treated with KI, none was found with normal aorta, and 2 showed marked calcification of the aorta.

Of 27 rabbits treated with KCNS, 15 were found with normal aortas, 3 with the aorta changed, 6 with slight calcification, and 3 with marked calcification of the vessel walls.

It may be interesting to note here also the occurrence of ascites in these experiments; we found that 15 of the 90 rabbits on which autopsies were performed showed this condition. It appeared through all the various sets, appearing once in the control sets (Series III), once in the iodipin sets (Series I), once in the iodipin and potassium iodide sets (Series II), 6 times in the potassium sulphocyanide sets (Series I, and Series II), and 7 times in the bromipin sets (Series 1 and Series II).

Hemorrhagic gastritis occurred in 11 of the cases and of these, 6 were in rabbits treated with potassium sulphocyanide (Series I and Series II), 2 were in the control sets (Series I), 2 in the bromipin sets (Series I), and 1 in the iodipin set (Series I). The occurrence of gastritis seems to have some connection with the administration of KCNS.

There was also noticed in 9 cases (Series I, Series II, and Series III) a peculiar condition of the left ventricle, a blanching and hardening of a portion of the muscle of the left ventricular wall, this area lying approximately midway between the apex and the base of the ventricle and being of various sizes. When the heart was exposed before it ceased its contractions it was noted that such indurated areas failed to take part in the contractions. The presence of these areas of myocarditis did not seem to be concomitant with the appearance of vascular changes due to adrenalin, or if such changes were present, simultaneously, with the degree of these lesions. These lesions have been recently studied by Pearce.[7]

In regard to the histological changes we may, on the whole, refer to the description given in the paper by Loeb and Githens. The main additional facts are the following: (1) Injection of any of the chemical substances used in this work with adrenalin does not influence the histological character of the lesions produced. (2) Especially noteworthy in our specimens were a number of slides from an animal treated with iodipin and adrenalin showing the aorta broken, the break passing through the intima and media, and a polypoid fibrin thrombus attached to the site of this lesion; the blood had infiltrated the space between the media and adventitia and formed there the beginning of a false aneurysm. (3) In another animal treated with adrenalin, iodipin, and potassium iodide the

[7] Experimental Myocarditis, Jour. Exp. Med., 1906, vol. viii.

blood had infiltrated the diseased media at some places, separated the elastic lamellæ and formed red-stained hyaline masses between the elastic fibers, the muscle nuclei disintegrating in this mass. (4) Van Gieson's stain, which was used among others in the preparation of these specimens, seems to have certain advantages over others. In good sections the periphery of the lesion in the media is clearly differentiated from the surrounding healthy parts by a red-stained area enclosing the necrotic yellow centre. (5) As Loeb and Githens stated in their paper, around the calcareous plates and places of necrosis we not rarely find a larger collection of nuclei than in other parts of the bloodvessels; this is perhaps due to the mechanical pressing together of the muscle nuclei about the site of the lesion. (6) In 1 case after iodipin and adrenalin injections, in which the aorta was normal to the naked eye, the aorta was likewise found to be normal under the microscope; it was, however, observed in this case, on microscopic examination that although the aorta was normal, one of the large vessels coming off from the arch of the aorta was markedly changed, showing even calcareous plates.

In a microscopic examination of sections of the heart from areas showing the above-mentioned myocarditis, we note mainly degenerative myocarditic lesions.

As a main result of the histological examination of our specimens we regard the fact that neither iodipin, KI, nor KCNS produce the slightest variation from the usual lesions produced by adrenalin.

With the above results before us we are led to the following conclusions:

1. It is not possible, by the use of various iodine preparations, to prevent the arterial changes produced in rabbits by the injection of adrenalin. No beneficial effect of the iodine preparations was noted in our experiments.

2. When large doses of iodine preparations were injected the arterial changes produced by adrenalin were more marked than when adrenalin was used alone. Our experiments suggest that iodipin acts less strongly in this direction than does potassium iodide.

3. Injections of potassium sulphocyanide in either fair-sized or relatively large doses did not cause an increase in arterial lesions produced by adrenalin. Our experiments point rather to the possibility that potassium sulphocyanide exerts a preventive influence on the action of adrenalin in producing arterial lesions; we cannot state this fact with any degree of positiveness, for in view of the uncertainty and variability of the action of adrenalin our experiments are hardly sufficiently extended to draw a positive conclusion.

4. Iodipin has no advantage over bromipin in preventing the vascular lesions of adrenalin, and in none of these series (combination of adrenalin and iodipin or bromipin) do we find the lesions less marked than when adrenalin was used alone.

SO-CALLED HYSTERICAL AFFECTIONS OF THE ABDOMEN.

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I desire herewith to report two interesting cases, illustrating the diagnosis of certain affections presenting signs referable to the gastro-intestinal canal, and serving to illustrate the differential diagnosis between organic disease and gastro-intestinal hysteria. I am indebted to Dr. Stuart McGuire for the privilege of reporting the cases.

Case I.—Miss. W., aged nineteen years. Her father died of paralysis; her mother of cancer of the stomach; one aunt, aged thirty-eight years, died in May, 1905, after an operation for an abdominal tumor. There is no functional nervous disease in the family. The patient is the youngest of seven children, and aside from the ordinary mild infections of childhood was healthy until she was nine years old. She had pleurisy at the age of ten years, which confined her to bed four or five weeks; and whooping-cough four or five years ago. For the past five years she has had "dysentery" every summer, but was never confined to bed until 1905. (This was while she was affected with the present trouble.) For two or three years she thinks she has been the victim of ulcers of the bowel. She was never constipated until the onset of the present trouble. She uses coffee in moderation. For the past three years she has kept house steadily for her brother, but never did much work and never cared for "society." Menstruation appeared at eleven years of age. This function has been slightly irregular in time of appearance and the flow was often scanty or profuse from no apparent cause, but until the onset of the present trouble she never missed a period. For two years she has had occasional leucorrhœa. Almost ever since puberty she has been the victim of frequent "hysterical" paroxysms, characterized by screaming, crying, and apparent unconsciousness, sometimes lasting two or three days.

In January, 1903, while apparently in good health, she began to suffer severe, generally distributed abdominal pain, more marked in the right iliac fossa. This was colicky in character and associated with violent screaming and crying, but with no nausea or constipation, and no fever, as far as is known. For this she was blistered on her abdomen and back and kept in bed three weeks, during which time she improved; since then she has never been entirely well. In May, 1903, she had a second attack, from which she has suffered ever since, frequently having been confined to bed; within the past year has been a "semi-invalid." Throughout, her digestion has been in no way impaired and she has never vomited

more than twice, and then from some such cause as improper diet or drugs.

In January, 1905, she was operated upon by a skilful surgeon for appendicitis, after which she remained in the hospital eight weeks (six weeks in bed). For two weeks more she was unable to walk on account of disability in the right lower extremity, and throughout convalescence her left arm was weak. Three weeks after going home (eleven weeks after the operation) the incision scar began to bleed (?) slightly and this kept up for a week. She then went to the country for two weeks to recuperate.

In May, 1905 (about this time her aunt died after an operation for abdominal tumor), she noticed for the first time that her abdomen was swollen. For this reason she consulted a physician who said he suspected "tumor and peritonitis," and referred her to another surgeon. The latter administered chloroform and told her upon recovery that the swelling entirely disappeared during anesthesia and that she had a "phantom tumor." She then returned to the country, where she remained six weeks. The swelling meanwhile persisted. Upon her return home she was attacked by "dysentery," which confined her to bed four weeks, during which time she suffered in addition to the abdominal swelling, abdominal pain, nausea, and vomiting. In August, 1905, she passed blood (?) from her bowels, on one occasion amounting to two tablespoonfuls (?), and once or twice after violent retching she noticed a little blood in the vomit.

On December 8, 1905, she became acutely constipated. For this she was confined to bed one week, and given purges, including jalap and croton oil, with little effect. After the administration of these she would be nauseated. Her bowels could be moved only by enemas. These were administered daily and followed each time by twenty-minute electric current to the abdomen. This treatment was kept up for nine days. Ever since this she has taken large enemas almost daily and often two or three times a day. The fecal material generally has been of liquid consistency (after enemas), though it is often well formed and in masses of normal size. A few times the bowels have moved without enemas. On the whole, since December, 1905, constipation has been obstinate, though there have been intervals during which it has been less marked, and for the past few days enemas are quite efficient. Defecation for months has been painful. Her appetite on the whole is good, but varies. Fruit acids are craved. Her usual weight is 135 to 140 pounds, and there has been no appreciable loss.

While convalescing from appendectomy she was unable to void urine for fourteen days, during which time she was systematically catheterized. In December, 1905, while constipated, she had to be catheterized twice, and again twice while she was being treated by electricity, but not since. The catheter was passed without difficulty.

There is generally severe pain, often lasting five minutes, at the end of urination. No hematuria has been noticed.

Since appendectomy was performed she has menstruated properly only three times, the last two times being in October, 1905, and January, 1906. At these periods the flow was free and apparently normal in duration. At other periods she has had only a very slight pink "stain." At each menstrual period, however, she has uterine colic and all the usual phenomena but the obvious flow. The hypogastric pain is more severe at each period than previously, and in February, 1906, confined her to bed one day. "Hysterical" paroxysms of crying and screaming have been frequent until the last two months, and for these morphine has occasionally been administered. She has been examined vaginally three times while conscious and this is neither pleasant nor painful. She has never had a sexual orgasm. She sleeps lightly and dreams much. On the whole she is miserable, but seems to have no apprehension of fatality of her affection. She is anxious to be cured, but does not desire to take chloroform, saying it makes her extremely nauseated. She says she abhors the idea of being operated upon.

Physical examination shows a well-developed, well-nourished young woman of good intelligence, refined and cultured manner, congenial and kind temperament. She is placid, gives fairly concise statements in her history, and is particularly exact in dates. She attributes most of her trouble to the operation, and her chief complaint is of obstinate constipation and abdominal swelling. The pupils are dilated, the face slightly flushed; she shows no evidence of pain, is comfortable in bed and perfectly able to walk. The plantar and patellar reflexes are exaggerated, but [illegible] reflexes are elicited. There is a capillary pulse [illegible] and on the forehead.

The abdomen is greatly distended, but the distraction is more marked below and above the umbilicus, with prominent hypogastrium, epigastrium, and flanks. At the level of the umbilicus there is a transverse constriction at the location of the lineæ transversæ. The circumference at the level of the iliac crests is 34½ inches, at the costal margin 27½ inches, and at the umbilicus 30¼ inches. Breathing is costo-abdominal in type and can be made wholly abdominal without undue effort or the slightest difficulty and does not produce pain. There is a small white scar over the appendicular region. The abdominal wall is held in extreme rigidity. In each iliac fossa and above the symphysis, tenderness is complained of upon deep palpation. In all parts of the abdomen rigidity can be overcome by prolonged broad pressure while she breathes deeply with her mouth open, shoulders elevated, and thighs flexed. The abdominal aorta, iliac arteries, and ascending and descending colon, can be palpated. No signs of free fluid can be elicited.

The distention gives the appearance of meteorism. This con-

clusion is confirmed by percussion, a tympanitic note being present all over the abdomen, save in the region of the liver. Hepatic dulness extends to the costal margin. Splenic dulness is not demonstrable. There is no abnormal area of circumscribed dulness, and no percussion tenderness. Auscultation reveals general exaggerated gurgling sounds due to peristaltic movements, though the latter are not visible. No fetal heart sounds nor movements are audible.

The rectal tube, finger, Kelley's large cystoscopic tube, and the proctoscope may be inserted into the rectum with difficulty. The latter meets marked resistance about 2 or 3 inches from the skin, but this is finally overcome and no further obstruction is noticed. The mucous membrane shows diffuse redness and obvious engorgement of vessels and is covered with mucous. There are many small erosions. The canal throughout contracts forcibly against the end of the instrument and the internal sphincter is greatly hypertrophied. One small, tender, and engorged hemorrhoid is seen at the mucocutaneous junction and the external sphincter is unusually tight.

Inspection of the external genitalia shows nothing abnormal, save slight leucorrhœa and hyperemia and a small urethral meatus. The clitoris is flaccid and normal in appearance. The hymen is present. Digital examination fails to detect any signs save great rigidity.

The heart, lungs, skin, lymphatics, bones, joints, and other structures are normal.

Immediately after the vulvar and rectal examinations the patient sunk into a stupor during which she was relaxed, breathed easily except for occasional spasmodic efforts and her pupils were dilated. There was no muscular twitching or crying. She responded to pain caused by flexion of the great toe and the passage of rectal instruments and was aroused without difficulty and made to walk around.

Diagnosis. Profound psychic hysteria; voluntary abdominal wall rigidity; general intestinal tympany; spasmodic stricture of the rectum; proctitis with erosions; inflamed mucocutaneous hemorrhoids; spasmodic amenorrhœa.

During chloroform anesthesia the abdominal distention entirely disappeared. She was allowed to regain consciousness and the distention reappeared.

Upon exploratory abdominal incision everything in the abdomen was found, upon careful examination, to be normal. During her stay in the hospital several weeks under active treatment for the psychosis, enemas had to be administered constantly, though occasionally a spontaneous bowel evacuation occurred. The distention persisted, though at intervals from no apparent cause, it would be slightly less marked. Since leaving the hospital she is apparently well.

This case affords a striking illustration of abdominal hysteria of profound type. The spasmodic stricture of the rectum may have

been hysterical in origin or a reflex result of the painful hemorrhoids and proctitis.

CASE II.—Miss Y. Her father, mother, two brothers, and one sister are living and well; there is some paralysis among her uncles, and her grandfather died of tuberculosis. She has had the ordinary infections of childhood, including diphtheria; pneumonia twice, the last time six years ago. About four years ago, at the time of her graduation from school, she had a mild attack of dysentery, confining her to bed a few days. She has always led an active life and was always remarkably healthy. She has taught school during the past four or five years.

In the latter part of the fall of 1902, while visiting away from home, she was seized one evening, while dancing, by an attack of severe colicky abdominal pain, nausea, and vomiting, so that she had to give up dancing. This pain was attributed at the time to dietetic error; the next day she was comfortable, save for general abdominal soreness. Within the course of a few days she was tolerably well, except for marked constipation. During the winter there were occasional recurrences of such paroxysms, and constipation became so marked as to necessitate purges.

Beginning March 17, 1903, she suffered for about a month with paroxysms of intermittent violent pain of the type of intestinal colic attended by nausea, obstinate vomiting, marked constipation, great abdominal distention, and with it all she was completely prostrated. She was operated upon at her home for intestinal obstruction. Upon opening the abdomen no obstruction was found, but the appendix, slightly adherent, was removed. During convalescence from the operation the distention and other symptoms persisted, and constipation was absolute for seven days. Upon getting up she noticed persistent abdominal distention. Her physician treated her almost continuously, especially for constipation, and was forced to administer enormous doses of strong purgatives. Licorice powder would generally be fairly effectual. The distention has persisted, the constipation has become more marked, and she has frequently suffered violent acute paroxysms of pain, nausea, vomiting, and prostration. In January, 1904, not having improved, she was operated upon again and her uterus, slightly retrodisplaced, was suspended.

She has continued to suffer recurrent paroxsyms of violent pain, vomiting, and prostration. Abdominal distention has persisted and she has not had a proper evacuation of the bowels in three years. She has had to continue taking purges and enemas, and came to St. Luke's Hospital for treatment.

Collateral Facts in the History. She has frequently noticed the passage of a little blood by the bowels, and on two or three occasions this amounted to a "couple of tablespoonfuls" of dark and clotted blood; she has noticed none of this during the past six months.

The evacuations have been made up largely of mucus, at times very marked quantities and in large flakes, especially after the second and third enemas. Purges produce violent increase of pain; enemas and the passage of rectal tubes are agonizing. There is never the slightest evacuation nor desire for such spontaneously; frequently two or three enemas are required and these are only partially successful. There has never been a formed movement. She has been treated constantly for hysteria, and for several weeks was cared for in a sanatorium in New York for this neurosis.

On one or two occasions she had pain of similar type, but having the location and radiation of right-sided renal colic. Her physician has found leukocytes, red cells, and small quantities of albumin in the urine. For the past year she has had dysmenorrhœa, and the administration of purgatives occasionally precipitates menstruation. She is otherwise well and hopeful. She has had no fever or chill, nor been unconscious. There have been no crying paroxysms, convulsions, or stupor.

Upon admission to the hospital she was suffering a violent attack, with great distention, rapid pulse, and other signs of a moderate degree of shock. After several days and repeated efforts a partial evacuation from the lower bowel was secured. Some time later, during the course of vaginal examination, the rectum was found impacted with feces. Examination of the pelvic organs was negative. During the first two or three days of June, 1906, she again suffered a violent attack similar in character to the above. Always after taking cathartic pills she suffered violently.

She is a well-nourished, slightly pale young woman, of a congenial temperament, but somewhat discouraged as to her recovery. She presents none of the appearances of a hysterical subject and seems perfectly normal in every respect except the abdomen. This is markedly distended all over and there is a transverse constriction at the waist line, that is, just above the umbilicus. Respiratory mobility is unimpaired. Measurements are as follows: At the xiphoid cartilage, 30 inches; half-way between the xiphoid and the umbilicus, $28\frac{3}{4}$ inches; at the umbilicus, $29\frac{1}{4}$ inches; half-way between the umbilicus and the pubis $32\frac{1}{2}$ inches. There is some lordosis in the lumbar region, but this is due to prominence of the buttocks rather than to spinal curvature. There is slight general abdominal tenderness somewhat more marked on the right side. Nearly the whole of the colon is palpable, but none of the other abdominal organs can be felt. The abdominal rigidity is that only of distention. Percussion reveals a general tympany and diminished area of liver dulness; the splenic area cannot be outlined. There is no area of circumscribed dulness. Auscultatory percussion is entirely negative.

At this point a provisional diagnosis of incomplete intestinal obstruction was based on the following: (1) A history of recurrent attacks of violent abdominal pain attended with nausea, vomiting,

moderate shock (prostration), and a number of times followed by the passage of blood; (2) obstinate, almost absolute, constipation; (3) intestinal distention; and (4) hypertrophy of the colon.

On rectal examination, externally no sign of the disease is seen; marked pulsation of the hemorrhoidal arteries is noted, and the rectum is empty. The passage of a proctoscope is attended by agonizing pain, in spite of the previous administration of a pint of olive oil. There is an area about 8 inches from the external sphincter in which there is greatly exaggerated tenderness and distinct resistance to the instrument, though this is finally overcome and the instrument passes 16 inches into the bowel. Inspection reveals an apparently sessile growth projecting into the lumen of the canal just above the junction of the sigmoid and the rectum. The mucous membrane of the rectum is moderately red, but shows no sign of localized disease and is empty. The sigmoid contains a small quantity of fecal matter and its mucous membrane is thrown into folds and apparently hypertrophied. There are no ulcers and only moderate inflammation. There are no signs of hemorrhoids, fistula, or fissure. The examination was agonizing to her. though she bore it bravely. The colic and local pain induced by the examination persisted until 4 P.M., at which time it was relieved by $\frac{1}{12}$ grain of morphine administered hypodermically.

Diagnosis. Incomplete intestinal obstruction; benign tumor of the colon?

Cœliotomy was performed June 11, 1906, by Dr. McGuire. The large intestine was distended with gas and feces; the rectum was empty. The sigmoid was found attached by a very short mesosigmoid causing sharp angulation of this tube. The colon above this point was filled with fecal matter and the rectum was empty. After dividing the short mesosigmoid the feces were easily manipulated into the rectum. Continuing the examination there were noted some adhesions of the omentum about the stomach. From the sense of touch it was impossible to find any lesion of the mucous membrane.

What we believed to be a growth arising from the mucous membrane as seen through the sigmoidoscope proved to be an invaginated portion of the mucous membrane of the sigmoid flexure through the portion pulled upon by its short mesentery and causing angulation of this part of the gut. The uterus was held anteriorly by an artificial ligament about an inch long resulting from a previous ventrosuspension. The old scar was dissected and the abdominal wall united in layers.

Convalescence was uninterrupted and on the third day following the operation a painless bowel evacuation was secured by the administration of 2 drams of extract of cascara followed by a simple enema. At the present time she is entirely free from symptoms. This woman had been treated three years for hysteria.

REVIEWS.

PEDIATRICS. THE HYGIENIC AND MEDICAL TREATMENT OF CHILDREN. By THOMAS MORGAN ROTCH, M.D., Professor of Pediatrics, Harvard University. Fifth edition. Pp. 1060. Illustrated by numerous engravings in the text and by colored plates. Philadelphia and London: J. B. Lippincott Co., 1907.

THE necessity for a new edition of Dr. Rotch's well-known text-book, according to the preface, "has afforded an opportunity to introduce many changes designed to bring the subject-matter up to the standard required by recent advances in the investigation of disease and the modern methods of treatment." The work upon the third edition, however, had been so thoroughly done that Dr. Rotch has really found little to change.

The division on feeding naturally has received the greatest attention, and the most recent advances in our knowledge of the chemistry of milk and the physiology of digestion have been incorporated in it. It is interesting to note that Dr. Rotch's attitude toward home modification has become distinctly less hostile than of yore, even though his championship of laboratory feeding is, and rightly, quite as enthusiastic. Top-milk feeding receives scant courtesy and Chapin's useful little dipper is not even mentioned. The subject of whey modifications has been considerably elaborated and their use is advocated as preferable to cereal attenuants.

One of the most important changes is the adoption of an etiological basis of classifying diseases of the gastro-enteric tract, those of the stomach and of the intestines being separately divided as they are developmental, non-infectious, or infectious, with intestinal worms as an independent class. This seems to us a distinct advance over previous systems of classification and worthy of general adoption for its simplicity and scientific accuracy.

A few changes have been made in the terminology of diseases of the kidneys, as the substitution of "acute degeneration of the kidney" for the older and less accurate term, "acute hyperemia."

Some necessary additions have been made in the section on diseases of the blood, and the term "articular rheumatism" is banished in favor of "rheumatic fever," as laying too much emphasis upon the articular manifestations of what is actually a general infection. New sections upon atrophic and hypertrophic diseases of the

joints and upon infectious arthritis, with a short section on the hypertrophic pulmonary osteo-arthropathy of Marie, about complete the changes to be found after a very careful comparison of the old and new editions. We may also call attention to the emendation which has been consistently made throughout the revision by the substitution of the plural of the first personal pronoun for the singular, an alteration presumably dictated only by the author's modesty, but which destroys to a considerable degree the inspiration of the personal note that has been such an attractive feature in Dr. Rotch's previous writings. T. S. W.

A Manual of Obstetrics. By A. F. A. King, M.D., Professor of Obstetrics and Diseases of Women in the Medical Department of the George Washington University, Washington, D. C., and in the Medical Department of the University of Vermont. Tenth edition. Pp. 688, 30 illustrations, and three colored plates. Philadelphia and New York: Lea Brothers & Co., 1907.

When, as in the case of King's *Manual of Obstetrics*, the publishers announce that it begins its second quarter-century with its tenth edition, what more need a reviewer say? The hypercritical are disarmed by the passage of time; commendation seems almost superfluous, since few books, and no other obstetrical book extant, can claim such a record. Dr. King's abilities and long service as a teacher have brought him into intimate personal relations with a large proportion of the practitioners of this country; indeed, he is now teaching the sons of some of his earlier students. To others he has become well and favorably known by his book—which in its tenth edition must claim an even wider circle of friends. The general scope of the work remains, as from the first, elementary, the main object being such brevity and simplicity of statement as might be easily intelligible to all students. In the new edition the chapter on fecundation and nutrition of the embryo has been almost entirely rewritten; extensive changes have been made in the chapters on pelvic deformities, cutting operations upon the mother, mutilating operations upon the child, placenta prævia, and puerperal septicemia; and minor alterations have been made elsewhere throughout the book. It is a pleasure to commend a work which, in addition to the authority and dignity of age, exhibits also the freshness of rejuvenescence, and to hope that Dr. King in the future, as in the past, may continue to issue new editions of his really excellent *Manual*.

A. K.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica, Jefferson Medical College; assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine, Jefferson Medical College, Philadelphia. Vol. I, March, 1907. Pp. 280. Philadelphia and New York: Lea Brothers & Co., 1907.

THIS, the first volume of the series for 1907, opens with a splendid chapter, one hundred and twenty-one pages, on recent progress in the surgery of the head, neck, and thorax, by Charles H. Frazier. Of the many important subjects discussed the following seem especially worthy of mention: Intracranial injuries, which includes an excellent discussion of 530 fractures of the base of the skull; Crile's method of controlling hemorrhage during operations on the head; the operability of cerebral tumors, including the technique of different operations; the treatment of cerebral abscess and of tumors of the hypophysis and the cerebellum; the surgical treatment of epilepsy and trifacial neuralgia; the treatment of carcinoma and syphilis of the mouth and tongue; the technique of operations on the neck; diseases of the thyroid and the parathyroid, including a discussion of the results of Kocher's latest 1000 thyroidectomies; carcinoma and other tumors of the breast, including a new method of removing the breast; the diagnosis of infections of the mediastinum; the surgery of the lung; and the results of sixteen recent cases of suture of the heart. Robert B. Preble discusses recent progress in infectious diseases, devoting special attention to the role of insects in the transmission of different infectious diseases; the importance of blood cultures in the diagnosis of certain infections; a report of 561 cases of diphtheria; the antitoxic treatment of dysentery; an excellent discussion of some recent contributions to epidemic cerebrospinal meningitis; pneumonia; rheumatic fever; scarlet fever; tuberculosis; typhoid fever, etc. Floyd M. Crandall, discussing diseases of children, devotes special attention to the incidence of disease in children—a review of 1000 cases; infantile mortality; the urine of infants; the tonsils as portals of microbic invasion; hemorrhages in the newborn; nervousness in children; infant feeding; the management of infants during hot weather, etc. D. Braden Kyle discusses recent progress in rhinology and laryngology, devoting special attention to deflections of the nasal septum; the treatment of hay fever; disease of the maxillary sinus; syphilis of the nose and the upper air passages; nasal and pharyngeal growths; the treatment of pharyngitis; the bacteriology of a common cold; tuberculosis, etc. B. Alexander Randall, reviewing recent literature on otology, dwells especially upon diseases of the labyrinth; meningitis; brain

abscess; phlebothrombosis; middle-ear suppuration; mastoid diseases, etc. Throughout the work seems to have been done with care and discrimination; assuredly the volume will well repay careful reading.

A. K.

THE IMMEDIATE CARE OF THE INJURED. By ALBERT S. MORROW, A.B., M.D., Attending Surgeon to the Workhouse Hospital and to the New York City Home for the Aged and Infirm. Pp. 340; 238 illustrations. Philadelphia and London: W. B. Saunders Co., 1906.

THERE is always a place for a comprehensively written and well-illustrated book on the immediate care of the injured which can be put into the hands of those members of the laity who are likely to be called upon to administer the first treatment in the case of injuries, such as nurses, policemen, steamship officers, soldiers, superintendents of factories, etc. The great difficulty in this matter is to teach such persons not to be overconfident or attempt to do too much. Surgery is a subject in which a little knowledge is sometimes a very bad thing, especially when it is put into practice. The reader of the present volume should carefully consider the preface, in which it is distinctly shown that non-professional aid should be only temporary, and nowise supersede or take the place of proper medical or surgical attention. Another feature which should be carefully considered by the layman who undertakes to administer first aid is the questions of anatomy and physiology. One-third of the present volume is devoted to this subject, and it is presented in simple and comprehensive language. Considerable space is devoted to bandaging, and also to accidents and emergencies.

We have but one criticism to make, and that applies to the treatment of wounds. We do not feel that the author has laid sufficient stress upon the prime importance of surgically clean hands. This is the most frequent source of infection of all wounds, and the layman especially needs to have the fact impressed upon him. The method of cleansing the hands is mentioned in detail, but its importance is not dwelt upon sufficiently.

In every respect this book can be recommended as a reliable guide not only to the layman, but also to nurses and to recent graduates of medicine.

J. H. G.

OUTLINES OF HUMAN EMBRYOLOGY. By GEORGE REESE SATTERLEE, M.A., M.D., Instructor in Histology and Embryology in the University and Bellevue Hospital Medical College, New York. Pp. 173; 99 illustrations. New York: John Wiley & Sons, 1906.

THIS little book, designed by the author for use in the laboratory and as a means of rapid review, is one of a class begotten by the modern methods of overcrowding the medical student. To fulfil the demand for condensed or boiled-down information the book, without doubt, is of value, but in default of a series of detailed lectures or demonstrations with the microscope it would be wellnigh unintelligible. This is especially true of the chapters covering the earliest development of the embryo, where comparative embryology is introduced to such an extent as to make the vaguest possible impression as to what really probably does occur in the human animal. Of course, it should be remembered that it is extremely difficult to create a conception of this portion of the subject in the mind of the student without full detailed descriptions, and in this case these have been sacrificed to brevity. The later chapters, in which the development of the various organs is discussed separately, are handled more clearly than the earlier ones. The author's style is clear but overly concise, and it may be said that throughout there is a marked tendency to sacrifice all else to brevity and condensation. There are numerous evidences of hurried proof-reading, and some inaccuracies in measurement. The illustrations are clear, well reproduced, and in the main well chosen, but it is questionable whether the rather numerous photomicrographs are of much value to the class of readers for which the volume is designed.

H. R. A.

PSYCHOLOGY APPLIED TO MEDICINE. INTRODUCTORY STUDIES. By DAVID W. WELLS, M.D. Philadelphia: F. A. Davis Company, 1907.

THIS small volume of 130 pages is an attempt, as stated in the preface, "to bridge over the gap between psychology and medicine." The title would suggest a thorough correlation of the two subjects. In the bridging process, however, both subjects are connected in a superficial and unscientific manner. That branch of medicine to which psychology has been most extensively applied is treated with a lack of thoroughness and knowledge that is little short of amazing. As an example of this, on page 121 the author states that "neurasthenias are difficult cases to treat, as they are hard to hypnotize. The same applies to hysteria." It is, of course, well known that hysterical subjects are always selected for medical experiments on

account of the ease with which they yield to hypnotic suggestion. In another paragraph there is a quotation from a newspaper report of an interview with a New York doctor concerning "his reviving of a moribund patient who had called for him previously to sinking into the comatose state." The author's knowledge appears to be limited to his own specialty, ophthalmology, from which most of his illustrations and comparisons are drawn. The other branches of medicine are either entirely neglected or simply mentioned as quotations from articles by others.

A reviewer should be charitable with any book which attempts to widen the range of therapeutic measures. The application of psychology to the treatment of disease has been too much neglected in the past. There is, indeed, a crying need for just such a book as the title would indicate. This volume, however, does not only not fill this need, but is likely to have a pernicious influence on account of its lack of thoroughness and accurate information.

D. J. McC.

A Pocket Formulary. By E. Quin Thornton, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College, Philadelphia. Eighth edition. Pp. 287. Philadelphia and New York: Lea Brothers and Co., 1907.

The new edition of Thornton's *Formulary* has been improved in many particulars, and it has been revised throughout to conform to the new edition of the U. S. Pharmacopœia. This is of major importance, since in the new Pharmacopœia the strength of many potent remedies has been materially changed. In the formulary diseases are arranged alphabetically, facilitating ready reference. Special mention should be made of the indications for use appended to many of the formulæ, and the suggestions to a choice when several formulæ are given under the one heading. Due regard has also been given to the palatability and the compatibility of the different formulæ. The little book has subserved a useful purpose in the past; in its new and revised edition it should commend itself to a still wider circle of practitioners.

A. K.

A Text-book of Obstetrics. By Barton Cooke Hirst, M.D., Professor of Obstetrics in the University of Pennsylvania. Fifth edition. Pp. 915; 753 illustrations, 39 of them in colors. Philadelphia and London: W. B. Saunders Co., 1906.

Dr. Hirst's *Text-book of Obstetrics* has become so widely known and so highly prized that mere mention of a new edition suffices.

The many excellencies of the book are common knowledge, so that a detailed recital thereof is quite superfluous. In this the fifth edition many minor modifications have been made, but especial attention has been paid to recent advances in our knowledge of puerperal infection and gestational toxemia. Dr. Hirst's large and continuously broadening experience as an obstetrician fits him eminently to prepare a book upon the subject, which in this new edition must enlist the interest of an increasing number of practitioners.

A. K.

ATLAS OF CUTANEOUS MORBID HISTOLOGY. By MAX JOSEPH, M.D., Physician for Skin Diseases in Berlin, and J. B. VAN DEVENTER, M.D., Oberstabsarzt of the Netherlands East Indian Army in Batavia-Java. 53 colored figures. Chicago: W. T. Keener & Co., 1906.

TIME was, and that not so very long ago, when the student of cutaneous diseases had to depend upon the meager paragraphs to be found in text-books of dermatology and of general pathology for information concerning the morbid anatomy of the skin. But *nous avons changé tout cela;* cutaneous pathology is no longer an unexplored region and text-books and atlases dealing with this special field increase yearly, thanks to a host of earnest workers whose labors are not only illuminating the dark places in the pathology of the skin, but are teaching the general pathologist some things worth knowing.

In this new *Atlas of Cutaneous Morbid Histology* there are 53 figures in colors, representing 45 separate diseases, which are, for the most part, accurate illustrations of disease of the skin as seen under the microscope. In the text which accompanies the plates a brief account of the most important histological features, which characterize the diseases portrayed, is given. We notice that the authors have given a new name, hydrocystoma tuberosum multiplex, to the disease first described by Kaposi as lymphangioma tuberosum multiplex. We cannot feel as certain as the authors seem to be that this neoplasm is of sweat-gland origin.

The chief, indeed the only, adverse criticism we have to make of this atlas is that too many figures (more than a fourth) are devoted to comparatively uncommon affections, such as acanthosis nigricans, pemphigus foliaceus, psorospermosis follicularis vegetans (which, by the way, might have been much better named), ichthyosis hystrix, etc., while so common a disease as eczema is not represented at all, the figure bearing this title being, in fact, a variety of ringworm. This necessarily limits the usefulness of the atlas very much.

M. B. H.

PRINCIPLES AND APPLICATION OF LOCAL TREATMENT IN DISEASES OF THE SKIN. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital. Pp. 130. New York: Rebman & Co., 1907.

THE contents of this volume comprise a short series of lectures delivered to physicians at the New York Skin and Cancer Hospital. The book does not pretend to be a treatise on the local treatment of skin diseases, but it gives practical suggestions that are not ordinarily met with in text-books. The author, as is well known to the profession, has had an immense experience with these diseases, and therefore all that he says is of value. While the local treatment is especially death with, attention is everywhere directed to the importance of the internal treatment suitable to the case.

One cannot peruse the volume without learning much of the principles of treatment, and after all is said concerning drugs, *combinations, and formulæ, in stubborn, deeply rooted inflammatory* diseases of the skin, success will not crown the efforts of the physician if the principles of practice be neglected or ignored. For permanent relief the patient and not the disease is to be treated. The booklet is a sort of *vade mecum*, from which many practical points may be gleaned. It is indexed in such a manner that everything referred to can be readily found.

L. A. D.

A TEXT-BOOK OF OPHTHALMIC OPERATIONS. By HAROLD GRIMSDALE, M.B., F.R.C.S., Ophthalmic Surgeon and Lecturer on Ophthalmic Surgery to St. George's Hospital; Surgeon to the Royal Westminster Ophthalmic Hospital, London, and ELMORE BREWERTON, F.R.C.S., Ophthalmic Surgeon to the Metropolitan Hospital; Surgeon to the Royal Westminster Ophthalmic Hospital, London. Chicago: W. T. Keener & Co., 1907.

THE various operations upon the different ocular structures are clearly described in this work, simple diagrams rendering the descriptions easily intelligible. A feature of the book is the number of operations proposed by recent writers, which are fully described, with the authors' names. Thus twenty-three operations for cicatricial entropion are mentioned, with the names of their proposers, and most of these are described with sufficient accuracy.

The work for exhaustiveness and wealth of detail, of course, is hardly to be compared with Czermak's upon the same subject, but it will prove a reliable guide for ophthalmologists who desire a work in English dealing with operations upon the eye.

T. B. S.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Difference in the Physical Signs at the Pulmonary Apices.—SEUFFERHELD (*Beit. z. Klin. d. Tuberkulose*, 1907, vii, 65). Considering the importance which is being attached to even slight changes in the physical signs at the apices as an indication of beginning pulmonary tuberculosis, it is necessary to have well in mind the normal differences. In the examination of 120 apparently healthy individuals between the ages of sixteen and fifty, Seufferheld found in 90, or 75 per cent., a lower position of the right apex; in 71 cases, the difference between the two sides was 1 cm. or less; in 19 cases over 1 cm. In 30 cases the apices rose to the same level, but in 8 of these 30 cases the diagnosis of a lesion at one apex could not be definitely excluded. The lower position of the right apex was associated with a slightly tympanitic quality to the percussion note, and usually a little impairment. Expiration at the right apex was accentuated, prolonged, and in some instances approaching the tubular quality, in 97 cases, or 80.8 per cent.; equal on the two sides in 18, or 15 per cent. In 5 cases it was rougher and more prolonged on the left side, but all of these 5 belong to the group of 8 suspected cases. Increased bronchophony was noted on the right side in 26 cases, or 21.7 per cent.; on the left, in 2, or 1.7 per cent.; and muscle sounds, that is, sounds which were inconstant and could not be satisfactorily explained otherwise, in 12 cases, or 10 per cent. The breath sounds were different on the two sides in 7 of the 30 cases of equal position of the apices. In all other instances the difference in expiration followed the percussion differences. In those cases in which the variations were so marked as to arouse the suspicion of a pulmonary lesion, radioscopy and the orthodiagraph were resorted to. Of 33 cases examined, 30 showed an equal position of the two apices and 28 an equal transparency. The 5 cases

showing differences again belong to the group of 8 suspected cases. On inspection the right shoulder was noticed to droop a little when viewed from the front in a large percentage of instances, but as a rule there was no difference when viewed from behind. In these cases the clavicle ran more horizontally than on the left side, and by measuring the sternoclavicular angle Seufferheld has sought to get an index of these differences. Of 90 cases measured the left was larger than the right 53 times; the right larger than the left, 20 times; equal, 17 times. Anatomically, and as shown by the orthodiagraph, the pulmonary apices have an equal position. Seufferheld suggests three factors which may be of importance in changing the percussion note so as to simulate a lower position on the right side: (1) Scoliosis which is frequently noticed in the cervical region associated with drooping of the right shoulder; (2) the greater muscular development on the right side; and (3) the compression which occurs between the resistance offered by the liver to expansion and the rigid shoulder girdle. The tympanitic quality which so frequently accompanies the percussion note and the changes in the character of the breath sounds are referred to the arrangement of the bronchial tree, the higher point of departure of the right main bronchus and its shorter course before division and the higher point of departure of the eparterial bronchus and its closer relation to the apex.

The Dicrotic Pulse in Aortic Insufficiency.—JANOWSKI (*Ztschr. f. klin. Med.*, 1907, lxi, 121); NURNBERG (*ibid.*, 1907, lxi, 130).—It is characteristic of the typical collapsing pulse in aortic insufficiency that there is no recurrent wave on the catacrotic limb. The question arises if the diagnosis of pure aortic insufficiency would be compatible with the presence of a dicrotic wave. As is well known, dicrotism depends upon decreased tension of the arterial wall, and it will occur in the pulse if the conditions exist to produce a diminished tension. Such conditions are the acute infectious diseases, dyscompensation of the cardiac activity, vasomotor disease as in morbus Basedowii, and in certain special poisonings, as by amyl nitrite. When such conditions occur in aortic insufficiency, the pulse becomes dicrotic and this need not disprove the diagnosis. Goldscheider has recently published 3 cases of aortic insufficiency with dicrotic pulse and a systolic mitral murmur, 2 of the 3 cases showing at autopsy a combined aortic and mitral insufficiency. On the basis of thess cases and of the observation previously published by Geigel, Goldscheider considers the mitral insufficiency responsible for the dicrotism. Geigel's observation was on a young woman with aortic insufficiency who, during an attack of acute endocarditis associated with the development of mitral insufficiency, acquired a dicrotic pulse which became again typically quick, as during convalescence the signs of mitral insufficiency receded. Janowski points out that in all of these cases there was fever, and in order to decide which of the two factors is the more prominent each must be studied separately. He gives a large number of instances of combined aortic and mitral lesions with careful pulse tracings, and in none does the mitral insufficiency influence in the least the typical collapsing quality. In fever the pulse of pure aortic insufficiency frequently becomes dicrotic and Janowski believes this to be the cause of the dicrotism in the cases of Geigel and Gold-

scheider. He takes exception to Goldscheider's view that when the pulse of aortic insufficiency becomes dicrotic we can diagnosticate the establishment of mitral insufficiency. Nürnberg, on the basis of his observations, supports the view of Goldscheider. He considers four factors of importance in causing the dicrotic notch: The presence of mitral insufficiency, the presence of fever, the age of the patient, and the duration of the lesion, the two last factors being an index of the elasticity of the arterial wall.

The Nature of Diabetes Insipidus.—Seiler (*Ztschr. f. klin. Med.*, 1907, lxi, 1) communicates a fairly complete and extensive article dealing with the nature of diabetes insipidus. The work in many ways is a confirmation of the results of work of E. Meyer (*Deut. Arch. f. klin. Med.*, 1905, lxxxiii). Seiler's work, however, was done in the years 1903–04; so about simultaneously with the work of Meyer, and each is, therefore, confirmation of the other's results. Seiler's observations were made on 4 cases. The first one was a girl, fourteen years of age, who had suffered from a fracture of the skull, following which there was bitemporal hemianopsia and diabetes insipidus. It is probable that the injury to the hypophysis played no role, as the blood pressure was not increased. The second case was one of diabetes insipidus in a child of eight years, in which no etiological factor could be determined. The third case was in an eighteen-year-old man, in association with fracture of the base of the skull. The fourth case was in an hysterical girl sixteen years old. This was the only case in which the course was favorable, and in which marked improvement was observed.

The old view that diabetes insipidus is a disease in which there is increased excretion of urine without any disease of the kidney can no longer be held, and for some time many persons at least have believed that the condition is due to a disturbance of the kidney function. This view is based mainly on the experiments of Strubell, Tallqvist, Meyer, and others. It was to confirm this view that the observations of Seiler were undertaken.

The first observations consisted in the accurate administration of constant quantities of water at hourly intervals during the twenty-four hours of the day, with examination of each separate specimen of urine voided. It was found that the amount of urine passed at night is considerably larger than that passed by day, but that the specific gravity of all specimens is quite constant. Such a condition can only result from an anomaly of kidney function, and is entirely opposed to the view of a disturbance of absorption, since it is hard to see why absorption should occur more rapidly by night than by day. Next, comparative estimations were made of the urine in a case of diabetes insipidus as compared with that of a normal person, and the differences in excretion were observed after the administration of a large amount of water, 1½ liters, early in the morning. Results showed that there was much more prompt water excretion in the healthy child than in the one with diabetes insipidus. In the patient with diabetes insipidus the excretion of the excessive amount of water extended over a longer period; in the healthy child the increased excretion was very quickly manifested, within a few hours. This, too, speaks for a disturbance of kidney function, unless it depends

upon a disturbance in water absorption. To see whether it is due to a disturbance of absorption, accurate estimations of the hemoglobin, by means of the Fleischl-Miescher hemometer, were made before and after drinking the large amount of water. It was found that in the patient with diabetes insipidus, just as in the healthy person, there was quite a marked diminution in the amount of hemoglobin in the blood, and therefore a thinning of the blood, appearing twenty minutes after the drinking of the water. From this it is quite evident that the delayed water excretion in the diabetic patient, as well as the increased amount of night urine as compared with day urine, cannot be due to delayed absorption, but must depend upon disturbance of kidney function.

A second series of observations was made to determine the nature more accurately of the disturbance in kidney function which occurs in diabetes insipidus. First, the quantitative estimation of the uric acid excreted; second, of urea; third, of posphates, and fourth, of chlorides, was made. Under ordinary circumstances there was no variation in what is considered the normal twenty-four-hour amount, except in the case of uric acid, in which there was a definite and quite marked diminution.

Further observations were made to determine the rapidity of excretion of certain urinary constituents. For this purpose, at a certain time during the day, large amounts of one of the various constituents of the food was administered and the effect of this upon the various urinary constituents was determined. In these experiments careful controls were made with the normal. In the first experiments the effect of the administration of large amounts of albumen was tested. The patient received in the morning five eggs, and afterward hourly observations of the urine were made. Now, while in the healthy the taking of five eggs was followed in from four to six hours by a marked increase in the specific gravity of the urine, which must depend upon an increased urea excretion, such a result did not occur in the case of diabetes insipidus, but there the increased excretion of urea occurred gradually, without any real change in the concentration of the urine. Next, an increase of carbohydrates in the shape of levulose and dextrose was given, without, however, there occurring any abnormal behavior of kidney activity under these conditions. The excretion of large amounts of salt was studied by the administration of large amounts of potassium iodide and the observation of the rate of its excretion in the urine. With the patient taking the ordinary amount of water, no apparent difference in excretion, as compared with that in the normal person, occurred. While Seiler lays no stress upon the excretion of methylene blue as an indication of normal or abnormal kidney function, he nevertheless made observations in order to render his experiments complete, and showed that methylene blue was excreted in the same way in the diabetes insipidus case as in the normal, except for a slight lessening in the time of excretion.

Now a series of more exact metabolism experiments was undertaken, in which the nourishment remained constant and the amount of water administered was varied. With the patient taking all the water he desired, the metabolism protocol showed no marked variation from the normal, except the diminution in uric acid previously mentioned. The

amount of water was then limited, and a control experiment was made on a healthy child. In the healthy child it was found, in confirmation of the observations of Neumann, that with an increase or diminution in the amount of water administered, nitrogen loss or retention occurs for the first one or two days, and that after that the figures are about those as before the change was made. In the diabetes insipidus case, however, following the restriction of water, the results were different. The amount of nitrogen excreted remained permanently diminished, and the same was true of chlorides and phosphates. The amount of uric acid excreted was in all conditions about the same, constantly under the normal. Also the excretion of potassium iodide under these conditions of water restriction was delayed, and, while with active diuresis the total amount of potassium iodide excreted through the kidneys was 65 per cent., with restriction of the water it was only 28 per cent. With the restriction of water, also, the patient experienced certain symptoms, such as headache, lassitude, disturbance of appetite, and tendency to vomiting, symptoms which were similar to those of beginning uremia. With a diminution in the amount of fluids given, there also occurred a definite increase in the osmotic pressure of the blood serum.

All these observations point quite definitely to diabetes insipidus being due to a disturbance of kidney function; that is, that the kidneys are no longer in a position to excrete a urine above a certain concentration, which concentration is usually considerably less than the normal. A satisfactory excretion of the organic and inorganic constituents of the urine then only takes place when such an amount of water is given that the urine will be of low concentration. If this amount of water is not given, the retention of the solid constituents occurs, and symptoms appear which are similar to those of uremia. The body, therefore, requires an increased amount of water, which the patient recognizes by increased thirst, and so arises the main symptom of the disease—polydypsia. Seiler draws attention to the possibility that the polyuria associated with contracted kidney may in its ultimate nature be the same as that of diabetes insipidus; that in both cases the polyuria is a compensatory mechanism, enabling the body to get rid of the solid waste products satisfactorily. In one case the disturbance of kidney function is due to an interstitial nephritis, and in the other it depends upon nervous conditions, at present unknown.

The therapeutic indications in this condition, therefore, are not the limitation of the amount of water administered as is so frequently recommended, but an attempt to stimulate the kidney to excrete the solid constituents in a more concentrated condition. Theoretically, therefore, the use of diuretics might be indicated. Experiments were made with the administration of caffeine, agurin, and theocine, but with none of these, however, were satisfactory results obtained. It was impossible by these means to obtain any greater or more active excretion of the solid constituents. With theocin the excretion of urea was both absolutely and relatively diminished. It is, therefore, evident that this drug might do more harm than good. Seiler lays stress upon the necessity in the indiviudal case of finding the optimum amount of fluid to be administered, and warns against the danger of a large increase or diminution above or below this amount.

A New Test for Sugar.—FENTON (*Lancet*, 1907, i, 215) outlines a new test for sugar which may be applicable in urinary examinations in certain cases, especially as it enables one to distinguish the hexoses from the pentoses or other lower sugars. The test is of great delicacy, but requires some little skill in manipulating. By it as low as 0.2 per cent. or less of sugar in the urine can be detected. The reaction depends upon the fact that all carbohydrates of the hexose or polyhexose type (such as dextrose, levulose, cane sugar, milk sugar, or maltose) yield a certain amount of bromomethyl-furfural, $CH_2BrC_4H_2O\text{-}CHO$, when acted upon by hydrobromic acid under appropiate conditions; and, further, that the latter substance reacts with malonic ester in presence of alkalies, giving rise to a product the solutions of which exhibit a powerful blue fluorescence. The test is as follows: Pour 4 to 5 c.c. of urine on an excess of solid anhydrous calcium chloride so as to form a semisolid or pasty mass. Add 10 c.c. of toluene containing 2 to 3 drops of phosphorus tribromide, and boil for a few minutes (bearing in mind the inflammable nature of the toluene). Pour off the toluene solution and, after cooling, add 1 c.c. of malonic ester and a little alcohol. On neutralizing with alcoholic potash a characteristic pink color occurs. The mixture then should be diluted considerably with alcohol and a few drops of water, when it will give a beautiful blue fluorescence if sugar be present.

The Pathogenesis of Congenital Icterus in the Adult.—CHAUFFARD (*La semaine médicale*, 1907, No. 3, 25) reports the case of a young man, twenty-four years of age, a brunette, and of a somewhat delicate build, whose skin and conjunctivæ were jaundiced. There was no family history of jaundice or of liver trouble. When very young he had diphtheria and at twelve years of age was extremely weak and anemic. This was followed a year later by an increase in the jaundice. At eighteen he had abundant and repeated epistaxis during the warm weather. The jaundice had been noted by the father of the boy after birth and had persisted steadily, but at times was more or less pronounced, being striking after fatigue or while travelling. The effect of any diet on the jaundice was not noticed. He did not take alcohol. As a rule, the patient was not sick, but at times after fatigue he had severe, cramp-like pains in the abdomen and increase in the jaundice. The stools were never clay-colored and the urine had showed only urobilin. There was no pruritus, no cutaneous hemorrhages or hemophilia. The reflexes were normal, pulse normal. Other organs were negative. The liver was not enlarged, but the spleen was quite large and hard. This enlargement was noted at the age of nine years, never disappeared, and remained the same up to the present time. Chauffard then gives a *resume* of the literature on congenital icterus, grouping them under three classes, in two of which the liver or changes in the bile-ducts are responsible for the jaundice, and a third group, to which the present case belongs, in which there were no changes in the liver. The history of this latter group starts with an article by Minkowski, "A Peculiar Hereditary Form of Splenomegaly with Chronic Jaundice, Urobilinuria, and Renal Siderosis" (*Verhandl. d. XVIII Kong. f. inn. Med.*, Wiesbaden, 1900). The most probable explanation, according to him, is that there is some

anomaly in the destruction of the blood, influenced by a primary lesion of the spleen. Other cases resembling this group are reported by Bettman; Gilbert, Castaigne and Lereboullet; Widal and Ravaut, Pick, and von Krannhals. (See AMER. JOUR. MED. SCI., 1905, cxxx, 721.) Chauffard then discusses two possible causes of this condition—(1) a persistent angiocolitis or (2) splenohemolysis—the first of which he dismisses on account of the clinical history of the case, its prolonged character, the few or only vague symptoms of an infection, the action of fatigue on the aggravation of the symptoms, and the condition of the liver in a case that came to autopsy, indicating little or no change in the biliary tract. He takes up the indications of hemolytic action in the reported cases and then passes to an extensive study of the blood in his own case, especially on the corpuscular resistance to hemolysis, following the work of P. Ribierre (*Thèse de Paris*, 1903) by the use of solutions of sodium chloride in different dilutions, and finds the hemolysis increased by comparison with other cases of simple jaundice and in those in which the liver is involved and not the spleen. Chauffard concludes that the predominating role in this condition is played by the spleen, and suggests that this study may lead to the recognition of the importance of splenohemolysis and the etiology of chronic jaundice in the adult.

Influenza.—The whole of volume lxxviii, No. 1, 1907, of the *Practitioner* is devoted to influenza, and contains seventeen articles by some of the celebrated English writers. DONALD ARMOUR, in his article on influenza and appendicitis, quotes extensively from the literature on this question, the most convincing statistics being those of Gagnière, who found that in 900 cases of influenza the percentage of appendicitis was about 1.3, these cases appearing during and ceasing, apparently, with the epidemic. BOTTOMLY notes an apparent increase in the number of cases of appendicitis during years when influenza was prevalent. The mortality from appendicitis appears to be increased during these years. According to other statistics this relation varies somewhat during different epidemics, being more prevalent when the influenza epidemic has many gastro-intestinal features. JOHN COWEN, in writing on the cardiac complications of influenza, notes that the myocardium is most commonly involved. The myocardial weakness is manifested by its usual train of symptoms, and the danger of sudden overstrain should be especially borne in mind. The treatment and prevention are then considered.

WILFRED HARRIS, in writing on the nervous system in influenza, divides the symptoms into: (1) Those at the onset, such as sudden faintness or syncope, headaches, severe general pains, sweats, and chills. (2) Those occurring in the course of the illness, meningitis, ocular disturbances, hysteroid convulsions, myelitis, Landry's paralysis, and neuritis. (3) Among the sequels, loss of the power of smell and taste, progressive bulbar paralysis, myasthenia gravis, epilepsy, loss of memory, and inertia of mind and body. T. CLAY SHAW, in discussing the psychoses of influenza, says the prognosis is good. "As a rule, the subjects, whether melancholic, maniacal, or stuporous, eventually and quickly recover, but a certain number do not and these go on to dementia or

remain in a more or less excited chronic condition. Upon all who are concerned with the treatment of influenza the obligation rests to remember that in proportion as the patient is neurotic or degenerate, or has a bad family mental history, so he is more likely to suffer from a postinfluenzal psychosis, which in a small percentage of cases may end fatally, and which is always a matter of solicitude, because of the tendency to relapse and of the frequency of suicidal influence."

Calcium Salts in Pneumonia and Heart Disease.—Sir Lauder Brunton (*Brit. Med. Jour.*, 1907, i, 616) contributes a short article on the use of calcium salts as cardiac tonics in pneumonia and heart disease. He refers to the discovery by Ringer of the beneficial effects of calcium salts on the heart. Brunton has had occasion to use calcium chloride in several cases of pneumonia with weak hearts, with apparently some beneficial results, and wishes it to have a wider trial. He prescribes it in 5 to 10 grain doses every four hours, and disguises the bitter taste by minute doses ($\frac{1}{20}$ grain) of saccharin to about 10 grains of the calcium salt. Brunton has used it also in cardiac cases with apparently good results. The chloride acts more quickly, but the lactophosphate or glycerophosphate could also be used. He thinks the good effects of a milk diet in some cases with heart disease may be due to the calcium salts contained in the milk.

Diagnostic Doses of Tuberculin.—Roepke (*Ztschr. f. Tuberkulose*, 1907, x, 412). The method of giving tuberculin for diagnosis according to the directions of Koch, namely, 1 mg., 5 mg., 10 mg., and again 10 mg. at intervals of two days, has been recently modified by employing much smaller doses. Loewenstein suggested giving $\frac{1}{5}$ mg. and repeating that amount four times, and Moeller, Ostrowsky, and other eminent authorities, after extensive trial, have approved the method. Roepke contends that such small doses are entirely insufficient and cites a number of instances in which no reaction has followed as many as five injections of $\frac{1}{5}$ mg. and appears in a perfectly typical manner when larger doses are resorted to. Some of these cases were known to have pulmonary tuberculosis; others were early, doubtful cases. He considers the method time-consuming and very unreliable, and returns with some modifications to the older procedure. The principal point of discussion is the maximum dose to which we must proceed. Koch's directions call for a repetition of the 10 mg. dose, and Bandelier insists upon following the directions faithfully. Other authors, as Junker, suggest stopping at 5 mg.; the latter's scale is $\frac{1}{10}$, $\frac{1}{2}$, and then 5 mg. Roepke, in a long discussion with many statistics, accepts a routine similar to this, giving $\frac{1}{5}$, 1, and then 5 mg. This gives results he believes as reliable as any other method, and shortens the time necessary for the test. One point of especial interest is the statement that he obtains signs of a local reaction in about 40 per cent. of the cases. This is an exceptionally large percentage.

SURGERY.

UNDER THE CHARGE OF

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The Technique of Narcosis.—STRAUCH (*Zentralbl. f. Chir.*, 1907, xxiv, 233) says that the use of chloroform is gradually becoming more restricted in favor of ether. He has employed morphine and alcohol as preliminaries to the anesthetization, as advised by Wenzel, but now prefers another method. Nothing affects more injuriously the heart strength than the continuous loss of sleep, anxiety, and excitement preceding operation, and in a large number of cases Strauch has found, on the morning of operation, arrhythmia of the pulse. That such a heart can offer no great resistance to the veil effects of chloroform is clear. To obviate this difficulty he gives to the patient, the evening before operation 1 gram of veronal. Even the most excitable women sleep, without exception, usually to be waked about an hour before operation, when they receive a hypodermic injection of morphine and a dose of alcohol. The veronal frequently continues to act, so that under its influence, with that of the morphine and alcohol, the patient is sleeping when brought into the operating-room, and is anesthetized quietly with a small quantity of ether given by the drop method. When necessary a few drops of chloroform are administered.

The Treatment of Pancreatic Fistulæ.—HEINEKE (*Zentralbl. f. Chir.*, 1907, xxxiv, 265) says that the two conditions that make these fistulæ so troublesome are the macerating effect on the skin of the pancreatic secretion and their persistency. To control the first, at the Leipzig Clinic, the siphon apparatus of Perthes for empyemas has been employed with excellent effect. The surrounding skin remains intact and the healing of the fistula hastened considerably. Wohlgemuth has shown that the quantity of pancreatic secretion produced depends upon the composition of the food taken. A pure fat diet produces the least, an albuminous diet a greater quantity, and a carbohydrate diet considerably increases it further. Acids increase, while alkalies decrease it. Wohlgemuth cured such a fistula in a short time by placing the patient on a diabetic diet and giving small doses of sodium bicarbonate. Heineke reports a case in which a similar result was obtained.

Subperiosteal Resection of the Diaphysis in the Long Bones.—SMOLER (*Ztschr. f. Heilkunde*, 1907, xxviii, 1) describes his method of operating as follows: The diseased diaphysis is exposed by a longitudinal incision so placed as to do as little damage as possible to the muscles, vessels, and

nerves. The periosteum is then carefully separated from the bone and the bone is resected by a chisel or a Gigli saw, the epiphysis being avoided in young people. It has been his practise to pack the wound with gauze and to apply to the extremity a wooden or a metal splint. In limbs with one bone, by this method, it was difficult to preserve the correct line in the reformed bone, and thus to obtain a good functional and cosmetic effect. The employment of weight and extension for the same purpose is associated with difficulty in the change of the dressings, and causes the patient much pain. Smoler accomplishes the purpose by the use of an aluminum splint introduced into the wound, to bind together, to a certain extent, the two ends of the bone during the process of union. The presence of this foreign body, by its irritation, aids the periosteum in forming new bone. He does not employ absorbable material for the splint, and does not entirely close the wound, because sooner or later these are generally extruded. He has had no cases in which an insufficient regeneration of new bone occurred, as shown by the *x*-rays and the functional results. By the use of only a few sutures and large drainage tubes the discharge finds a free escape, and the wound may be washed out by a hydrogen peroxide solution. When sufficient regeneration of new bone has taken place the aluminum plate is sawed or broken with forceps into several fragments and is removed piecemeal through the drainage opening. A half-year or more was usually required for healing.

The Treatment of Undescended Testicle.—Lotheissen (*Ztschr. f. Heilkunde*, 1907, xxviii, 37) gives the following reasons for operating for undescended testicle: Pain and neuroses are frequent. Periorchitis occurs easily (from frequent trauma) and can prove dangerous. Hernia is frequently associated and may become incarcerated. Torsion of the cord may take place and lead to gangrene of the testicle, unless operated on promptly. Psychical disturbances are frequent on account of the "lack" of the testicle. Operation may permit the further development of the testicle, so that the earlier the operation is done the better. After it is done the patient may enter the army. The cosmetic effect deserves some attention. If the testicle is healthy, orchidopexia should be done, while castration should be reserved for a necrosed testicle or malignant degeneration of the testicle.

Lotheissen makes an incision as for an inguinal hernia, two fingers' breadth above Poupart's ligament, but extends it past the spine of the pubis to about the root of the penis. He then opens the inguinal canal as for a hernia operation, being careful not to injure the testicle or its bloodvessels. The hernial sac or tunica vaginalis is exposed and isolated from the surrounding structures as far as the internal ring, where it is ligated. It is then divided and removed from the testicle. The spermatic cord is then stretched carefully. Lotheissen has been able thus far to do this without excision of the vessels. The testicle is then placed in a cavity in the scrotum made with the finger, and is held there by a gauze tampon. The internal oblique and transversalis muscles, sometimes the rectus also, are sutured to the lower internal edge of Poupart's ligament, over the cord. The gauze tampon is then removed from the scrotum and the connective tissue is sutured over the cord, so that the whole cord is enclosed in a canal. It will be observed that as

the sutures are being introduced and tied the testicle is being forced lower until it reaches the lowest part of the scrotum. In bad cases it may remain a finger's breadth higher than on the opposite side. The external oblique fascia and the skin are then sutured. Care should be taken to avoid, as far as possible, infection by the urine.

Tumors of the Kidney in Children.—MOUCHET (*Annales des maladies des organes génito-urinaires*, 1907, xxv, 342) says that they are observed especially in the first years. Some of the tumors are of complex structure, formed essentially of embryonal elements, multiple tissues in a sarcomatous network. Some are true cancers, in the clinical sense of the word, and are rapid and progressive in development. The tumor element is the first and often the only clinical sign. Hematuria is rare and tardy. The volume reached is generally considerable. Death occurs, usually from cachexia, in a short time. Extirpation is difficult and grave. An early diagnosis and immediate operation are essential to the radical cure of a malignant tumor. The first is difficult because of the absence of the important symptom of hematuria. In operating the abdominal route should be preferred, but it is essential to have good light and to remove the tumor *en masse*, that is, the tumor, its fatty capsule and the glands, thus avoiding transplanting the tumor debris in the wound. The prognosis, however, for a permanent cure is so bad that one can say of them that the chief interest in these tumors concerns their anatomical structure.

Some Notes Apropos of Cases of Appendicitis Treated during the Years 1905 and 1906, in the Service of J. Verhoogen, in the Hospital Saint Jean.—GRAEUWE (*Jour. de chir. et Annales de la Société Belge de chirurgie* 1907, vii, 140) says that 36 cases were treated in this time, with 2 deaths, or a mortality of 5.5 per cent. The 1 case of simple acute appendicitis was treated only medically and recovered. This consists of rest, an ice-bag locally, and no opium, except a hypodermic injection of morphine at the beginning of the attack, if the pain is acute. After some weeks without fever, and when there is no tenderness on pressure and the swelling has disappeared, the operation is usually done. An analysis of the blood is always made to determine the presence of an active suppurating focus. In some cases, as when the patient supports a family and the necessity for going back to work is urgent, he sometimes intervenes in a shorter time, but even in these only after the fever has disappeared some days. In all cases from the time of their entrance into the hospital, numerous leukocyte counts are made. It is especially in the cases with localized peritonitis that these counts are valuable. In these there is a high leukocytosis during the first days, which increases as the abscess progresses and decreases as the abscess diminishes. If, in an acute case, there is marked rigidity and a daily increase in leukocytosis, operation is done immediately. The abscess is opened and drained with rubber tubes and gauze. Irrigation of the cavity of the abscess is not practised for fear of infecting the general peritoneal cavity. The search for the appendix is made with care. If it can be liberated without too great separation of adhesions it is removed, if not it is left in place.

If, on the other hand, the leukocytes decrease and the general condition

remains good, operation is delayed. Thanks to the examinations of the blood he has never had cause to repent for having operated too hastily or too tardily. In cases of generalized peritonitis, with anxious expression, frequent vomiting, and irregular pulse and temperature, operation is done immediately. After resection of the gangrenous appendix a free discharge of the pus is provided for by several incisions, which are left largely open and through which are introduced large drains surrounded by iodoform gauze.

The Pathology of the Effusion in Traumatic Serositis.—MERCADE and LEMAIRE (*Revue de chirurgie*, xxvii, 396) find that the lymphatic elements are the dominating factor in the effusion, the blood elements being of so negligible a quantity that we may infer that in some cases it may be wholly lacking, only the lymph remaining. They conclude, therefore, that the traumatic effusion is purely of lymphatic origin, aside from that blood which comes from rupture of the capillaries, and which at the end of some days is well mixed with the lymph elements.

Pylorectomy in Benign Stenoses of the Pylorus.—BRECHOT (*Revue de chirurgie*, 1907, xxvii,.471) says that the gravity of a pylorectomy varies with that of the lesion of the pylorus for which it is done. It is followed by immediate results, as good as those of gastro-enterostomy, in those cases in which the resection is easy. The later results are not as troublesome as those of gastro-enterostomy, nor do the complications arise, often fatal from the evolution of the causal lesion. When a pylorectomy is impracticable, a gastroduodenostomy should be done, since it gives a more physiological result than a gastro-enterostomy. The latter will be necessary when the two previous operations cannot be done. The duodenum is an essential organ in digestion. It permits the passage only of the necessary quantity of chyme. It controls the intestinal and pancreatic secretions. Brechot gives a series of cases, personal and from other writers, to show—that the evolution of the ulcer is not arrested by gastro-enterostomy; the dangers of the operation; the influence of a secondary resection; and the necessity of resecting the ulcer, and reëstablishing the gastro-intestinal canal.

The Perineal and Freyer's Transvesical Prostatectomies.—CASTANO (*Annales des maladies des organes génito-urinaires*, 1907, xxv, 401) says that the suprapubic is more easily executed than the perineal prostatectomy. It has the great advantage of exposing the bladder to direct examination by sight, and of facilitating the extraction of vesical lobes and calculi, so frequent in these cases. In total prostatectomy, which should always be done, the perineal operation sacrifices the posterior urethra, while it is left intact in the transvesical. Catheterism is very easy after the transvesical; after the perineal sounds must be passed for some time to shape the urethra. The duration of the transvesical operation is shorter and the rectum is in less danger. Impotence and epididymitis are rare in the transvesical and common in the perineal operation. The great advantage of the latter is the better drainage afforded, and when it is impossible to disinfect the bladder Castano considers this operation preferable. The functional results are more

rapid after the transvesical operation, urination being soon spontaneous and complete. Aside from the severely infected cases, Castano believes that the results obtained from the Freyer operation are on a par with and probably better than from the perineal.

The Incision for Appendectomy and Lateral Celiotomy.—Baracz (*Zentralbl. f. Chir.*, 1907, xxxiv, 330) says that partly as a result of his visit to America, in 1902, and partly as a result of his own experience, he considers the McBurney incision preferable to all others in preventing ventral hernias. He is convinced that it is of great service in other operations in the lateral abdominal regions, as for the making of an artificial anus in the cecum or sigmoid flexure, a better sphincter being obtained than by the other incisions.

The After-treatment of Operations for Cancer of the Breast.—Ewald (*Zentralbl. f. Chir.*, 1907, xxxiv, 385) suggests a method of after-treatment in these cases which aims to reduce limitation of movements in the shoulder following these operations. The affected arm is not bound to the side of the body in the usual manner, but is held in abduction beyond a right angle, by means of a traction apparatus. This can be made by adhesive plaster wrapped about the wrist and hand, which grasps a suitable piece of wood from the two ends of which a cord or bandage attaches the hand to an apparatus fixed above the head of the bed and projecting toward the affected side of the body. An additional support is applied under the arm just above the elbow. The patient is kept in this position for three or four days, and after that the arm is gradually lowered until when the patient is ready to leave her bed it is at the side. Whenever she goes back to bed the arm should be again raised in the abducted position. By this method Ewald found that except in excessively obese individuals, the patient, two weeks after operation, could place her hand on her head by her own strength. The stretching of the skin over the axillary space, in this position, prevents the collection of blood or lymph in the cavity made by cleaning out the axilla.

Spontaneous Abdominal Herniæ through the Semilunar Line of Spiegel.—Thevenot and Gabaurd (*Rev. de chir.*, 1907, xxvii, 586) say that the diagnosis concerns itself particularly with the volume of the hernia. If it is small the patient complains only of the functional troubles, as dyspepsia, enterocolitis etc. On account of the fixed pain associated with it, one thinks on the left side of a sigmoiditis, and on the right side of a cholecystitis or a chronic appendicitis, according to the height of the hernia. The hard mass in the abdominal wall makes one think of a fibroma, lipoma, or abscess. The diagnosis, usually, will be made only by the reducibility, impulse on coughing, etc. If the hernia is large, the diagnosis is usually easy, and it should then not be confounded with an inguinal or umbilical hernia. The treatment is essentially the same as that of an umbilical hernia.

An Anatomicopathological Study of Dislocations of the Semilunar Cartilages of the Knee.—Dambrin (*Rev. de chir.*, 1907, xxvii, 616) says that in recurrent dislocations operation is necessary, as well as in recent dislocations that cannot be reduced by the usual manipulations. The

operation is at the same time benign and efficacious. It consists either of an arthrotomy with fixation of the cartilage, meniscopexy, or extirpation of the cartilage, meniscectomy. The incision is a vertical one, about 6 cm. long, and about midway between the patella and the internal lateral ligament, with its centre over the interarticular line. This avoids wounding the important internal lateral ligament. The cartilage is then sutured to the periosteum of the tibia or is removed. In comparing the results of the two operations Dambrin says that both are equally easy, and while both are very benign extirpation is more so than fixation. Of 87 extirpations there were 4 in which very mild infection occurred, while of 35 cases of fixation there were 5 in which joint infection occurred, 1 of which was prolonged. This difference is accounted for by the prolonged manipulations in placing the sutures in fixation and the presence of the sutures as foreign bodies. In 53 of the 87 extirpations absolute cures were obtained. Lenail found in dogs that the meniscus was regenerated after its removal. Dambrin does not believe that this occurs. From the point of view of efficaciousness, the results of extirpation of the cartilage are easily superior to those of fixation.

Transportation of the Sartorius Muscle as a Means of Fixation in Excision of the Knee.—KOFMANN (*Zentralbl. f. Chir.*, 1907, xxxiv, 417) says that posterior flexion of the knee as a late result of excision is a well-known condition. None of the many methods of excision which have been devised have succeeded in overcoming this difficulty. Heusner recommended the transference of the flexors of the knee to the anterior surface of the knee. Kofmann tried this several times and felt that he had done too much. He concluded that in his next case he would merely transplant the sartorius as Schantz had done for dislocation of the semilunar cartilage. In this case he made a median incision through which he exposed and prepared the sartorius from the middle of the thigh to its insertion into the anterior surface of the tibia. He then made a transverse incision from the end of the first incision over the tuberosity of the tibia to the lateral ligament, thus opening the joint. This was the seat of a partly fibrous and partly bony ankylosis. The patella and the ends of the femur and tibia were removed to permit the placing of the limb in extension, and the sawed surfaces were kept approximated by silk sutures through the periosteum and cartilage. The sartorius was then attacked. It was easily seen that it was so loose that it was unnecessary to isolate the muscle, but that a little loosening was sufficient to permit displacing it from its normal lateral position to one directly over the front of the joint. Three sutures secured it over the rectus muscle. Kofmann satisfied himself of the effective strength of the displaced muscle by lifting the extremity by the heel, the bones remaining in position without any support. The skin sutures were introduced, and the dressing and a plaster cast were applied. They were removed in eight days; healing was by first intention; a lighter cast permitted the patient to go around. In fifteen days all dressings were removed.

THERAPEUTICS.

UNDER THE CHARGE OF

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The X-rays in Diseases of the Blood and Blood-forming Organs.—PANCOAST (*Univ. Penna. Med. Bull.*, 1906, vol. xix, No. 11) reports his own observations upon this subject and gives a review of the literature. In regard to leukemia he finds that of 63 patients reported, only 4 (6.35 per cent.) are still alive and well three to six years after the primary symptomatic cure. He assumes that it is safe to assert that, were the final reports at hand of all patients that have been treated by the *x*-rays, this percentage would be but slightly altered. In 39 patients, or over 70 per cent. of those that died or are at present in critical condition, there was either a very marked amelioration in the symptoms or a symptomatic cure, as a result of the treatment at first. In view of these results, Pancoast considers that the Röntgen ray can hardly be held to be a specific in leukemia and that the effects of treatment by it are not very encouraging. He asserts that the dangers attending the use of the rays should be remembered and evidences of toxemia should be looked for; frequent urinary examinations should be made to determine the extent and rapidity of tissue destruction and the state of the kidneys. There is clear evidence that death has been caused or hastened by failure to observe these points. In favor of the treatment of pseudoleukemia by means of the *x*-rays Pancoast mentions the following points: (1) A cure for at least three or four years may be obtained in about 25 per cent. of the patients treated. (2) In almost all instances not so cured, life is prolonged during a period of comparative comfort by improvement in the general condition or by the relief of pressure. (3) No other agent can yield as good results. (4) By further improvements in technique and a better understanding of the pathology of the disease, even more favorable results than those obtained at present may be possible. In the treatment of polycythemia by the *x*-rays the results cannot be considered very favorable. In the absence of more definite knowledge it would seem that the rays should be applied over the splenic area. Twelve instances of splenic anemia have been collected by Pancoast in which improvement due to the employment of the Röntgen rays has been noted. With regard to pernicious anemia the statement is made that before subjecting the patient to the rays, even for the purpose of skiagraphy, except in urgent necessity, metabolism investigations should be carried out in conjunction, and the physician must be sure that there are no evidences of

toxemia and that other forms of treatment are unavailing. Unless these precautions are taken the results may be of the most untoward character.

The Roentgen Rays in Mediastinal Tumor.—ELISCHER and ENGEL (*Deut. med. Woch.*, 1906, No. 40, p. 1620) report 3 instances of mediastinal lymphoma treated with the *x*-rays. They conclude that if the tumor is directly retrosternal it is most amenable to this mode of treatment. In the first patient after eight treatments of from five to ten minutes' duration there was evident improvement; after sixteen sittings the patient, considering his cure complete, ceased treatment. One year later there were slight signs of recurrence, but the patient refused further treatment In the second instance the lesion seemed to be a tuberculous adenitis. The exposures brought about marked relief of the symptoms, but the tumor persisted A similar result was attained in the third patient, the nature of whose tumor was undiagnosticated. Four other patients are reported in whom the treatment was ineffectual; the tumor in these instances was possibly a lymphosarcoma. The authors consider that all mediastinal neoplasms should be submitted to radiotherapy; in many instances a rapid betterment will follow, and, if the tumor is simple lymphoma, a cure may be, perhaps, expected.

Quinine in Influenza.—BROADBENT (*The Practitioner*, 1907, lxxviii, 13) has held, since the first invasion of influenza, that quinine is the best remedy. He prefers to give it in a prescription containing 1 part of ammoniated quinine to 2 parts of liquor ammoniæ acetatis. Of this mixture the dose is 3 drams every hour for three hours and then every four hours. In the fulminating attacks of the disease, in which the patient has become comatose, quinine hydrobromide given hypodermically in large doses has relieved the unconsciousness. As a prophylactic the author orders 2 grains of quinine every morning during the prevalence of epidemics and considers that he gets good results; although patients who were taking quinine occasionally contract influenza, in many instances this makes a complete difference in the patient's liability to infection.

The Treatment of Serous Pleurisy.—FORCHHEIMER. (*Jour. Amer. Med. Assoc.*, 1907, xlviii, 28) considers that the longer fluid is allowed to remain in the pleural cavity the greater the likelihood of the formation of adhesions, that it is a risk for the patient to go about his ordinary pursuits with the effusion, for dangerous symptoms may develop at any time, and finally if the fluid is withdrawn the process may be terminated. These Forchheimer considers strong arguments for early paracentesis, and he would not wait for the occurrence of the symptoms of intrathoracic pressure. He also advocates withdrawal of the fluid in tuberculous pleurisy since, after tapping, an artificial hyperemia, following the pressure anemia previously existing, occurs and good effects, as claimed for it by Bier, take place. The hyperemia also induces a leukocytosis, which is followed by the development of connective tissue which tends to encapsulate the tubercle. He makes the definite statement that paracentesis should be performed eight days after compression of the lung has existed, and as much fluid as possible should be drawn off, for the more fluid withdrawn the greater the hyperemia.

The Treatment of Hay Fever.—BELBEZE (*La province médicale*, 1906, No. 34, p. 404) gives the following list of the drugs useful in this affection: Cocaine, stovaine, or adrenalin with cocaine, applied to the inferior turbinates; cologne-water or lavender-water, either combined with menthol or pure, by inhalations; stramonium by inhalation or in cigarettes; vaseline with menthol, applied directly or as a spray; ammonium chloride as an inhalation. Cocaine and stovaine should be employed with caution on account of the possibility of habit formation. In the prophylactic treatment of the condition the author advocates the use of sodium cacodylate for about a month previous to the time when an attack is expected. Intranasal conditions should receive appropriate treatment, and potassium iodide is also useful as a preventive when given in doses of about 8 grains daily for two or three weeks before an anticipated seizure.

The Treatment of Eclampsia.—LAURANDEAU (*Jour. de med. de Paris*, 1906, No. 38, 412) advises in addition to the usual means—chloral, chloroform, the bromides, etc.—doses of 15 drops of fluid extract of veratrum, which may be accompanied by hypodermic injections of $\frac{1}{60}$ grain each of scopolamine hydrobromate and morphine hydrochloride, given deep into the muscles of the thigh and repeated in thirty minutes if necessary. Two hours later, if the symptoms persist, a third injection and a second dose of veratrum may be given. Laurandeau advises against exceeding these doses. The alkaloid veratrine may be substituted. The inunction into the abdomen of an ointment consisting of veratrine 7½ grains, cocaine hydrochloride 6 grains, vaseline one ounce, is also suggested.

PEDIATRICS.

UNDER THE CHARGE OF

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Alcoholic Cirrhosis of the Liver in Children.—ERNEST JONES (*Brit. Jour. of Children's Diseases*, January, 1907, p. 1) prefaces a critical study under this caption by reporting two personal cases of unusual interest. The first was that of a Russian Jewess, sixteen months old. She was brought to the hospital for manifestations of malnutrition of three or four months' standing, and was gradually getting worse. The mother had been in a hospital in St. Petersburg for several months and the child had been cared for by its grandmother from the age of eleven months. During the whole of this time the child had received a little wine twice a day; the amount of the dose varied, but was frequently a tablespoonful. Wasting, vomiting, looseness of bowels, and slight jaundice were the prominent symptoms. There was a little fluid in the peritoneal cavity; the liver was enlarged, reaching to within an inch of the umbilicus,

its edge sharp and hard. The spleen was just palpable. The course of the disease after treatment was begun was very favorable, and recovery took place. The second case was that of an English girl, three years old. She had had pertussis, which had begun six months previously and had lasted three months. Toward the end of that time brandy had been prescribed in doses of a dram twice a day. This amount was exceeded to a variable extent and was continued for over five weeks. There was considerable fluid in the peritoneal cavity, and the liver extended three or four fingers' breadth below the costal margin; the spleen was not palpable. The subsequent course of this case was very favorable. Jones has collected 72 other cases from the literature as a basis of a very careful analysis of some of the points concerning this condition. As to frequency of incidence the available statistics show that the greater frequency of the condition in adults is by no means so pronounced as is generally supposed. The commonest source of the alcohol—in over half the cases—was the parents, who usually gave it with the good intention of improving the child's condition—for debility or minor ailments. In the rest of the cases the commonest source was the medical practitioner, and in 3 of the cases the medical attendant specifically ordered an increase of the habitual alcoholic beverage with the idea of treating the malnutrition due to the unrecognized cirrhosis. In conclusion Jones expresses the opinion that the evidence as to the importance of alcohol in the causation of hepatic cirrhosis in children is sufficient to justify our taking the possibility of its production into consideration when ordering alcohol or permitting its employment in the case of children who are amenable to the influence of our advice.

Hot Intestinal Injections in Enterocolitis.—CARAVASSILI, of Athens (*La Clin. Infant.*, August, 1906, p. 475), advocates the use of hot intestinal injections in enterocolitis as being more efficacious than simply warm injections or other local measures. The temperature should be from 104° to 107.6° F. Colic and spasm are diminished and sometimes entirely suspended for from four to nine hours after such an injection, and then reappeared generally in much less severe degree. The character of the stools is promptly improved and their frequency diminished after each injection, and usually the number required does not exceed from three to six for any given case.

Statistics of Diphtheria from the Paris Hopital des Enfants-malades.—Since assuming direction of the diphtheria pavilion of this hospital in 1901, MARFAN (*Revue mensuelle des maladies de l'enfance*, April, 1907, p. 180) has had published each year, by one of his internes, the statistics of his service. These reports, which have been made successively by Weill-Hallé (*Soc. méd. des hôp.*, June 12, 1903), Leenhardt (*ibid.*, January 22, 1904), Detot (*ibid.*, December 2, 1904), Le Play (*ibid.*, December 8, 1905), and Henri Lemaire (*ibid.*, February 15, 1907), are of extreme value to anyone making research of the literature of diphtheria, and illustrate strikingly the efficacy of the antidiphtheritic serum. Previous to 1894, when the serum was first employed, the mortality from diphtheria in all the Paris hospitals for children averaged

50 per cent. As compared with this the following statistics for the years from 1901, in Marfan's service, are peculiarly significant. By reduced mortality is to be understood that calculated after the exclusion of cases dying in less than twenty-four hours after admission. For 1901–02, 1122 cases, total mortality 21 per cent., reduced mortality 12.3 per cent.; for 1902–03, 1048 cases, total mortality 15.8 per cent., reduced mortality 11.1 per cent.; for 1903–04, 605 cases, 14.2 and 9 per cent.; for 1904–05, 561 cases, 7.6 and 5.47 per cent.; and for 1905–06, 534 cases, 10.11 and 6.97 per cent.

In explanation of the higher figures of the first two years it is stated that toward the end of 1900 a very severe epidemic of malignant diphtheria prevailed and that the usual number of cases treated was more than doubled, and that this epidemic lasted until near the end of 1902. From these statistics Marfan believes the mortality from diphtheria depends particularly upon the frequency of malignant anginas. As accessory factors in the mortality must be considered the number of croups necessitating intervention, the frequency of bronchopneumonia, and that of certain associations, as shown in the slight increase of the mortality observed in 1905–06, depending upon the frequency of association with measles. It is to be understood that the accuracy of these observations presupposes the methodical employment of the antitoxin, the lack of which, Marfan believes, stands as the principal factor in the mortality of the disease.

Purulent Meningitis and Empyema of the Frontal Sinuses in the Course of Eruptive Fevers.—SCHOLLE (*Arch. f. Kinderheilk.*, 1906, xliv, 306) reports two observations, one of measles and scarlatina in a boy of ten years and one of scarlatina in a girl of six years, in both of which death ensued from purulent meningitis consecutive to empyema of the frontal sinus, which was discovered only at the autopsy. In both cases the inflammation of the frontal sinus had been so intense as to cause obstruction of the nasofrontal canal and to prevent the outflow of pus by the nose, which would have pointed to the correct diagnosis. In the first case the pus accumulated in the right frontal sinus was under great pressure, since the child presented during life an œdema of the right eyelid and exophthalmos, symptoms which where wrongly attributed to a thrombosis of the venous sinuses consecutive to a suppurative otitis which existed at the same time. As diagnostic signs Scholle suggests tenderness on pressure on the floor of the sinus, occasionally with a sensation of yielding of the wall and a flow of pus into the nose; and redness after percussion over the sinus, more marked and persistent than over the sound side.

The Duration of Immunity after Injections of Antitoxin.—SITTLER (*Jahrb. f. Kinder.*, 1906, xiv, p. 442) bases this study upon 912 cases at the Children's Hospital at Strassburg immunized by an injection of 500 units; 700 of these were healthly children, the brothers or sisters of 378 diphtheria patients; 212 were scarlatina patients, who were in a different ward from the diphtheria cases. Of the 700 cases 4 contracted diphtheria sixteen hours, thirteen days, five weeks, and six weeks respectively after injection. Of the scarlatinal cases only 1 developed

a mild diphtheria three days after injection. Sittler comes to the following conclusions: (1) The prophylactic injection of serum produces an immunity of from three to five weeks or even longer only under the condition that the child is not brought in contact too often with diphtheria cases or convalescents from the disease. In case of such contact, when the child is constantly exposed, the duration of immunity is not greater than from ten to fifteen days. But under these same conditions non-immunized children contract the disease very much more frequently than those who have been immunized. (2) All catarrhal affections and others which affect the mucous membranes, even in immunized cases, constitute a condition eminently favorable to the development of diphtheria, and shorten at the same time the duration of immunity. (3) After diphtheria occurring in children who have been previously immunized, a second attack of the disease may occur as early as with children who have only submitted to immunization. (4) Generalized scarlatiniform eruptions, even when they develop without fever and without marked angina, are most frequently true scarlatinal infections.

Serum Treatment of Diphtheritic Paralysis.—Comby (*Arch. de méd. des enf.*, August, 1906) reports further cases illustrating the value of antidiphtheritic serum in the treatment of diphtheritic paralyses. He advocates the free use of the serum, whether or not it had been previously used in the treatment of the primary disease. The dose should be large and repeated if necessary.

The Blood Changes in Mumps.—Referring to the difficulty in diagnosis encountered at times at the outset of a case of mumps, Ira S. Wile (*Arch. of Pediat.*, September, 1906, p. 669) states that a blood examination will positively determine the diagnosis in its earliest stage without waiting to observe its course. As a result of examinations in 20 consecutive cases he concludes that lymphocytosis, both relative and absolute, is noted on the first day of the disease, no matter how small the tumor may be, and continues until all swelling has disappeared. It is more marked relatively with bilateral involvement than with unilateral disease, and is most marked in children at puberty, though it is present in adult cases, but is less accentuated. Eosinophiles are slightly decreased in the beginning, but rise to normal or above during convalescence. The eosinophilia is higher in bilateral involvement than in the unilateral affection, as the period of convalescence begins at this time. The basophiles are not affected. The polynuclear neutrophiles vary relatively inversely with the lymphocytes. With orchitic complications the polynuclear neutrophiles tend to increase relatively, though there may be no absolute leukocytosis. Hyperleukocytosis does occur, but is not of high degree. There is no secondary anemia. Lymphocytosis is a diagnostic feature of mumps, differentiating it from adenitis. The average count of this series was: Lymphocytes, 59.37 per cent.; polynuclear neutrophiles, 38.32 per cent.; polynuclear eosinophiles, 2.28 per cent.; polynuclear basophiles, 0.43 per cent. It is important to remember that at one year the lymphocytes normally form 51 per cent. of the leukocytes; at three years, 43 per cent.; at six years, 38 per cent.; at eight years, 35 per cent.; and at nine years and over,

31 per cent. As cases of mumps in children under one year are very rare, it is a safe general rule to state that a relative lymphocytosis occurring in children to the extent of 50 per cent. or above is always pathological. The total leukocyte count may be said to vary normally from 10,000 to 15,000 in the first year and a half of life. After the second year the number approximates that found in adult life—8000. In adenitis, even from decayed teeth, there is a high leukocytosis in children—even as high as 43,000.

OBSTETRICS.

UNDER THE CHARGE OF

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The Induction of Labor for Disproportion between Mother and Child.—Moller (*Arch. f. Gynäk.*, 1906, Band lxxx, Heft 3) reports 80 cases of induced labor for disproportion between mother and child. The total number of births among which these cases occurred was 21,066; among these there were 646 contracted pelves, or 1 in 32.6, which is about 3 per cent. In all labors occurring in the clinic, induction was practised once in 277.2 cases; among the contracted pelves it was necessary to induce labor once in 8.73 cases. The most frequent type of contracted pelvis was the justominor. Labor was induced in 2 cases for contraction of the birth canal outside of the pelvis. In these cases the head presented in 67.5 per cent.; in 32.5 per cent. the breech presented. Among the cases of head presentation, 14 had unfavorable position of the cranium, and 10 of these were cases in which elastic bags had been used. Of these induced labors 52.5 per cent. terminated spontaneously, and 47.5 per cent. required an obstetric operation to complete delivery. The maternal mortality among these patients was 1.25 per cent. The maternal morbidity was 33.75 per cent., or 27 cases. Among these were 12 cases of pyuria, bronchitis, and mastitis; 7 of these patients had well-marked fever for at least one day, and 8 of them became septic. The calculated morbidity of the mothers was 20 per cent. Of the children, 18.75 per cent. were stillborn; the fœtal morbidity is not stated. Induced labor was thought indicated when the true conjugate was 7 cm. or thereabouts. The most favorable period on the average, for induction of labor, was thirty-five weeks of gestation. Vertex presentations were most favorable, and of these 90.7 per cent. were born living. When the breech presented 61.5 per cent. were born living. The principal dangers of induced labor arose from injuries to the birth canal, and also to the child during operative delivery which terminated in induced labor. A further difficulty lies in the uncertainty of the actual period of gestation, and hence the difficulty in choosing accurately the most favorable time for the induction of labor. When the results obtained by induced labor are compared with the results of allowing the patient to go on to spontaneous labor, it is found

that between two or three times as many living children are obtained after induced labor as after a spontaneous parturition. The children of induced labor, however, seem to possess but half the average strength of those spontaneously born. If children born by induced labor are followed for one year after birth it is observed that 20 per cent. less are living at the end of one year than of children born by other methods. The child's chance for life is diminished in accordance with the early period chosen for the interruption of pregnancy. Thus, before the thirty-fifth week the fœtal mortality is 10 per cent. greater than among children born by other methods.

Accidental Hemorrhage Complicating Pregnancy and Labor.—WRIGHT (*Amer. Jour. Obst.*, November, 1906) reports the case of a multipara, seven months advanced, who while driving was taken with severe abdominal pains. Four days afterward she expelled spontaneously a dead child, with large clots. The placenta had been half discharged. When the uterus is exceedingly thin, and accidental hemorrhage occurs, it enlarges by the gradual formation of retained blood clot. In such a case this gradual enlargement of the uterus and its softness would furnish a valuable diagnostic sign. Wright considers pain and shock as especially valuable symptoms in this complication. He cites an obscure case of a multipara at eight months, in whom pain and shock developed. There was considerable abdominal tenderness, which disappeared after the bowels had moved freely, the patient ultimately making a good recovery. The treatment which he has found most successful consists in an enema of salt solution, sufficient morphine hypodermically to keep the patient perfectly quiet, strychnine $\frac{1}{30}$ grain, given not more than twice, keeping the patient's head as low as possible, and raising the foot of the bed. Especial attention should also be given to maintaining the heat of the body by external application.

The diagnosis of this condition is frequently especially difficult. It may be impossible before delivery to recognize clearly the condition. These patients rapidly become profoundly anemic; the uterus is distended in some to such an extent that it cannot be recognized by abdominal palpation. A condition of shock so severe may be present as to suggest a dangerous traumatism. When there is external as well as internal hemorrhage the diagnosis is more readily made. Retaining the blood within the uterus often produces effects difficult to recognize clearly. During the early stages of accidental hemorrhage blood clot stimulates the uterine muscle to contract, producing a condition of uterine tetanus. While this is present it is often impossible to recognize fœtal heart sounds or to map out the fœtus by palpation. If accidental hemorrhage follows severe traumatism the patient's shock becomes extreme. When hemorrhage without traumatism is present, the symptoms of collapse and loss of blood predominate. In the presence of considerable shock it is safest not to subject the patient to operation.

Suprarenal Extract in the Treatment of Osteomalacia.—BOSSI (*Ctralb. Gynäk.*, 1907, No. 6) reports a case of twin pregnancy complicated by osteomalacia in which the disease of the pelvis was successfully treated by the administration of suprarenal extract. He further reports

the case of a patient six months pregnant to whom the remedy was given by hypodermic injection. A practical cure of the condition was secured in twelve days. To test as far as possible the relation between disease or absence of the suprarenal bodies and osteomalacia, Bossi removed the right suprarenal body from a pregnant sheep. Osteomalacia developed immediately afterward.

Pregnancy after Sterilization by Atmokausis.—MEYER (*Ctralb. f. Gynäk.*, 1907, No. 6) reports the case of a multipara who had been treated by atmokausis for persistent uterine hemorrhage. The anterior wall of the uterus was greatly thinned and stretched, while the posterior wall seemed to have been greatly thickened by the treatment employed. The patient was about five months pregnant when vigorous bleeding came on. This was controlled by packing with iodoform gauze, and followed by operation. The case is interesting as showing that pregnancy is possible in cases in which the uterine cavity was supposed to have been obliterated by steam. Evidently the steam had attacked the posterior wall of the uterus and not the anterior. When pregnancy occurred and the ovum developed, that portion of the uterus not converted into cicatricial tissue became excessively distended and was, in fact, in danger of rupture. After atmokausis, not all patients so treated have obliteration of the uterine cavity. Fuchs in 18 of these cases observed obliteration in 11.

Multiple Sclerosis and Pregnancy.—WAGNER (*Ctralb. f. Gynäk.*, 1907, No. 6) reports the case of a primipara, aged thirty years, who forty-eight hours before admission to the hospital was attacked by cramps, which gradually developed into eclampsia. Paroxysms began in the region supplied by the right facial nerve, thence extending into the left upper extremity. The uterus was emptied under ether, and treatment addressed to the eclamptic condition was carried out. It proved, however, unsuccessful, the patient's strength failing until death occurred. At autopsy, multiple sclerosis of the brain and cord was present. The interesting question arises as to whether the convulsions depended upon the process from the brain and cord, or whether they were of the usual eclamptic variety, the lesions of the nervous system having nothing to do with the convulsions.

Cesarean Section for an Unusual Indication.—WECHSBERG (*Ctralb. f. Gynäk.*, 1907, No. 6) reports the case of a patient who came to the hospital in a pregnant condition, having a vesicovaginal fistula, the result of a previous difficult forceps delivery. After this the child died half an hour following birth. Repeated attempts had been made by operation to close the fistula, and this operation had been successful. During the last of her treatment the patient was found to be pregnant. After thorough examination, it was decided that delivery through the vagina would undoubtedly injure the urethra, and probably result in the formation of a fistula larger than the original. To avoid this, the patient was successfully delivered by Cesarean section.

GYNECOLOGY.

UNDER THE CHARGE OF

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Spontaneous Resection of the Tubes.—GUICCIARDI (*Ginecologia; Zentralbl. f. Gyn.*, 1906, No. 47, p. 1319) reports 5 cases of torsion of the Fallopian tube found in 1041 laparotomies and 3 in which spontaneous amputation had resulted. In the most typical a nullipara, aged forty-nine years, had a right sactosalpinx confined to the distal end. At a point an inch from the uterine cornu the tube was entirely separated, the ends being an inch apart. Guicciardi believes that the mechanical factors in producing this condition are gradual elongation, and torsion or constriction of the tube, especially if it be dilated at the distal end (ampullary sactosalpinx).

Movable Kidneys in Women.—HEIDENHAIN (*Therap. Monatshefte*, 1906, No. 2, p. 1320) adheres to the theory of Wolkow and Delitzin with regard to the presence of "paravertebral niches," the normal position of the kidneys being maintained only when these are of a certain shape. In cases of movable right kidney the niche is notably shallow. The maintenance of the intra-abdominal equilibrium is most necessary to maintain the organs in their normal position; and this is secured through the elasticity of the abdominal walls and viscera. In operating it is not enough to fix the kidney in its normal position. Heidenhain prefers Schede's method.

Operations for Diseased Adnexa.—In discussing this subject before the Dresden Gynecological Society (*Zentralbl. f. Gyn.*, 1906, No. 49, p. 1352, LEOPOLD referred to a previous communication by Osterloh in which he reported 111 operations, in 52 of which drainage was employed, 10 of the latter cases having subsequently intestinal fistulæ, 2 of which resulted fatally. Leopold himself lost 2 per cent. of his last 150 cases, and drained only 9, in 4 of which intestinal fistulæ developed, 2 healing spontaneously. One of the patients in whose case drainage was employed died. Leopold's inference was that it is better to dispense entirely with gauze drainage. His plan is after walling off the field of operation to aspirate thoroughly a pyosalpinx or ovarian abscess, to clamp the opening made by the needle, and then carefully to enucleate the sac, sponging away pus as it appears. Under these conditions drainage is superfluous even in the worst cases, unless it is impossible to check oozing, when gauze is used, not as a drain, but as a tampon. In the discussion which followed Weindler affirmed that drainage was an unfortunate necessity, indicated only when large dead spaces were left. Schobach believed in drainage per vaginam only in recent pus cases of a doubtful character or when large raw surfaces existed. He used xeroform gauze, the drain being removed in five days. He had lost 1 out of 42 patients thus treated.

Gonococcic Peritonitis.—Leopold (*Zentralbl. f. Gyn.*, 1906, No. 49, p. 1354) reported a successful case of abdominal section for puerperal peritonitis, being the first one in his clinic in which gonococci had been found in the peritoneal exudate. The operation was performed eighteen hours after the inception of fever, the cavity being flushed daily with normal saline solution through three tubes—one in either groin and the other inserted through Douglas' pouch. The first two were left *in situ* for three weeks and the other for two weeks longer. Extensive granulation of the wounds occurred, but these eventually healed after the use of the sharp spoon and the patient made a good recovery.

Uterine Fibroid Complicated with Cancer.—Bland Sutton (*Jour. of Obstet. and Gyn. of Brit. Empire*, 1906, No. 7), in a series of 500 cases, met with only 8 in which there was accompanying adenocarcinoma of the corpus uteri; hence his inference that the presence of the benign neoplasm does not predispose the patient to the development of malignant disease. In his experience this complication is most common in unmarried or sterile women between the ages of fifty and sixty years. In 2 of the 500 cases primary cancer of the Fallopian tube was found.

Piquard (*Ann. de gyn. et d'obstét.; Zentralbl. f. Gyn.*, 1906, No. 49, p. 1368) bases his deductions upon 1000 cases of uterine fibromyoma, in 15 of which cancer of the corpus uteri was found. He infers that the chronic metritis induced by the presence of a fibroid predisposes to the development of cancer. Piquard was able to collect 179 cases in all from the literature. In this connection he reports 45 cases in which epitheliomatous degeneration of a fibroid occurred, though the majority of these were secondary to malignant disease of the endometrium. Primary cancerous degeneration of a fibromyoma was noted in only 24 cases, which are explained on the theory of preëxisting epithelial cells, possibly of embryonal origin, derived from the Wolffian bodies or Müller's ducts. The explanation that inflammation of the endometrium covering the fibroid leads to proliferation and invasion of the neoplasms by glands that subsequently degenerate seems more plausible.

Secondary Ovarian Tumors.—Amann (*Münch. med. Woch.; Zentralbl. f. Gyn.*, 1906, No. 49, p. 1365), from a study of 18 cases, recognizes three varieties of secondary cancer of the ovary: (1) Œdematous fibroma, with epithelial foci; (2) adenocarcinoma with subsequent cystic degeneration; (3) ovarian cystoma with discrete scirrhous foci.

In the first class the cancerous cells are distributed in the form of columns, which penetrate the fibrous tissue and often undergo colloid degeneration. Histologically they frequently give the impression of being endotheliomas. The hyperplasia of connective tissue represents a reaction of the ovary against the invasion of the neoplastic cells. This condition was noted in cases of cancer of the stomach and other viscera in which the ovaries were macroscopically unchanged.

It is not always possible, according to Amann, to prove the secondary origin of the ovarian neoplasm, especially when a small cancerous nodule in the stomach is associated with a large malignant ovarian tumor, except for the well-known fact that metastases in the stomach do not occur in connection with cancer of the ovary.

As regards the second variety, he states that while primary adeno-

carcinoma may develop in the ovary, double colloid cancer of both ovaries is rare, though it is quite common as a metastasis of gastric or intestinal cancer. In the third class secondary infection is possible, but rapid growth of pre-existing ovarian neoplasms in connection with long-standing cancer of the stomach and the presence of areas of œdematous connective tissue furnish evidence of metastasis. Infection may occur through implantation of detached cancerous masses on the surface of the ovary (!) or, if the original neoplasm in the wall of the stomach or intestine has not perforated it by way of the lymphatics.

The practical deduction is that in all cases of probable malignant disease of the ovaries the stomach should be carefully examined. In the event of an explorative incision being made, the viscera should be thoroughly palpated, since the primary tumor may be so small that it may even escape attention at the autopsy.

Resection of the Urete.—ZWEIFEL reported a case before the Leipzig Obstetrical Society (*Zentralbl. f. Gyn.*, 1906, No. 43) in which he resected 5 cm. of the left ureter in connection with radical abdominal hysterectomy for cancer of the uterus, the proximal end being successfully sutured *into the bladder. Of four similar operations in his clinic three were* successful. In the discussion which followed Franz reported 17 cases of ureter resection, all but one in connection with extirpation of the cancerous uterus. Five patients succumbed to the operation. Of the twelve others (in two both ureters were implanted in the bladder) only one failed. Freund believed that when it was necessary to make extensive resection of the ureter high up it was better to avoid implanting the proximal end in the rectum or abdominal wound, or extirpation of the kidney, by uniting the end of the ureter with that of the Fallopian tube (uretero-salpingo-cystotomy). He had practised this method in dogs with good results. It is necessary to make a uterovaginal fistula afterward.

Ovarian Cyst with Chorio-epithelioma Metastasis.—SCHMAUS (*Beit. z. Geb. u. Gyn.*, 1906, Band x, Heft 2) reports a case of ovariotomy for adeno-carcinoma of the ovary, in which the patient developed, a year later, nodules in the peritoneum and omentum which presented the histological appearance of chorio-epithelioma. He regards these as metastases rather than primary neoplasms, because of the fact that the origina cyst contained cell-formations resembling the secondary growths.

OTOLOGY.

UNDER THE CHARGE OF

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The Results Obtained from the Radical Operation for Chronic Purulent Otitis Media.—EDWARD BRADFORD DENCH (*Annals of Otology, Rhinology, and Laryngology*, September, 1906) is of the opinion that, in the

matter of permanent relief of the otorrhœa, the results obtained by this operation are not as flattering as had been hoped when the procedure was first suggested. Out of 193 cases, there were 131 cures, 29 with slight discharge, 5 with profuse discharge, 2 were still under treatment, there were 6 fatal cases, and 20 cases in which the result was unknown. Of the 6 deaths, 2 patients died of pneumonia, 2 of meningitis, 1 of cerebral abscess, and 1 of cerebellar abscess complicated by sarcoma of the auditory nerve. In no instance could death be attributed either directly or indirectly to the operation. Including the cases operated upon several years ago, and followed carefully, the results have been most satisfactory. Even when a small amount of discharge has persisted for weeks or even months after the operation, this discharge has in almost every instance disappeared absolutely, without the necessity for secondary interference, under simple measures of cleanliness.

It is not uncommon to have the patients return, at intervals of from four months to one or two years, complaining of some discharge from the external auditory canal, the entire cavity being filled with a mass of desquamated epithelium, upon the removal of which a small amount of pus may be found. If this accumulation has remained in the canal for a considerable period of time, desquamation of the epithelial lining of the cavity may have taken place either completely or over certain areas. If the cavity is simply sterilized with an alcoholic solution of bichloride of mercury, and then dusted with some bland, non-irritating powder, such as boric acid, xeroform, zinc oxide, or, in fact, any sterile powder, the cavity becomes dry, the apparent relapse in many of the cases being due to the fact that the integument lining the middle-ear cavity and the mastoid cells, is improperly nourished, the integument forming the lining of a blind pouch being subjected to increased temperature, increased moisture, and deprived of light and of air, which are essential to the proper nutrition of the normal skin; this tegumentary lining, moreover, is applied closely to the bony walls of the cavity, with very little connective tissue substance intervening.

These attacks of desquamation occur less and less frequently, because the integument gradually adapts itself to its new habitat, and conforms itself to its anomalous position; they should not be looked upon as a recurrence of the otitis, since they are easily relieved by the removal of the walls of the cavity.

Out of 111 cases, in which the hearing records were kept, the hearing after the operation was good in 99, was fair in 9, and was bad in 3. Out of the last 95 cases operated on, facial paralysis occurred in 4 instances, and the function was ultimately restored in all.

As regards the technique of the operation, the author is in favor of the employment of large skin grafts applied, preferably, through the posterior opening, on account of the shortening of the after treatment.

Arteriosclerosis of the Labyrinth and Acoustic Centres.—E. ESCAT (*Annales des maladies de l'oreille et du larynx*, 1906, xxxii, 325) gives a most interesting paper that furnishes food for a great deal of thought on the part of otologists. He considers it astonishing that a study of the localization of arteriosclerosis in the ear has not sooner found a place in otological pathology. He chides the profession for not

having better applied general medical knowledge to the problems of special organs, points out some of the difficulties in the way of studying the pathology of the internal ear, and sets forth the proposition that "in the same way that a cortical centre of the brain, a pyramid of the kidney, an hepatic or splenic lobule, or a retina may suffer from arterial spasm or the cutting off of its nourishment, so may the labyrinth. The internal auditory artery, as well as the iliac or coronary, may suffer from hypertension and endarteritis. The study of otitic arteriosclerosis is exactly homologous with that of the eye."

A schematic drawing is presented to show the distribution of nutritive arteries to the labyrinth and to explain how, by the anatomical disposition of the arteries, arteriosclerosis may be limited to a single department of the auditory apparatus or may involve it extensively. He discusses the pathology of arteriosclerosis and points out that "the process would act the same on the labyrinth as on the acoustic centres, because, like the brain, it is but a peripheral expansion of the brain. The paroxysmal form of the syndrome of Ménière, with complete remissions, shows a crippling of the labyrinth by spasm of the internal auditory. The apoplectic form of the same syndrome with intralabyrinthine hemorrhage, is similar to rupture of an artery in cerebral hemorrhage or in epistaxis. Now, if degeneration of the coats of the terminals of the internal auditory causes hemorrhage it is also certain that endarteritis of the same vessels will lead to slow atrophy of the organ. The lesion may occur in the vestibule, semicircular canals, termination of the vestibular nerve, or the ganglion of Scarpa."

Clinically he divides the labyrinthine troubles caused by arteriosclerosis into three types: (1) Deafness without vertigo; (2) vertigo without deafness, and (3) deafness and vertigo associated.

"Arteriosclerotic deafness comes on slowly, insidiously, and is progressive; general arteriosclerosis may or may not have become evident; it is generally worse on one side than on the other; there is less impairment of perception of the low than of the high tones; bone conduction is shortened; the patient hears better in silence than in a noise. Objective examination may show but little evidence of change in the membrana tympani; occasionally there is a sclerotic white ring about the periphery, analogous to the arcus senilis of the cornea, but little importance can be attached to this. There is usually no evidence of ankylosis of the ossicles and nasopharyngeal examinations fail to disclose any sufficient abnormality to explain the impaired hearing. The diagnosis then rests upon the existence of a gradually progressive deafness, presenting the characteristics of a lesion of the perceptive apparatus, and, general signs of arteriosclerosis, such as hypertension and induration of the peripheral arteries. When the last-named elements are lacking the diagnosis is reduced to a presumption and must await confirmation by later developments.

"Deafness without vertigo will be produced by arteriosclerosis when the lesion involves the vessels or centres supplying the cochlea only, and leaves those of the vestibule unimpaired; the four principal foci, where this may occur, are the cochlear artery proper, the cochlear nuclei in the pons, in the posterior arm of the capsule, or the temporal branch of the sylvian artery. The slowly progressing form is due to obliterative endarteritis, the rapid form to emboli.

"Vertigo without deafness is capable of being produced by an arteriosclerosis in a region which affects the vestibular vessels or centres which control equilibrium, without coincident involvement of the cochlear circulation.

"Deafness and vertigo associated is much more commonly recognized, probably because it usually presents the syndrome of Ménière so clearly; that is, tinnitus and nausea are added to the above symptoms. Here the lesion is apt to be an arteriosclerosis of the internal artery itself and a consequent interference with both the nuclear and vestibular vessels. Labyrinthine hemorrhage or embolism will produce the symptoms rapidly, while a progressive sclerosis of the internal auditory artery causes a gradual development of the syndrome. Likewise, lesions in the cortex or pons that involve centres controlling the equilibrium will produce the complex type of the disease.

"The two conditions especially to be borne in mind when making a differential diagnosis are hereditary or secondary syphilitic labyrinthitis and otosclerosis. The hemorrhagic labyrinthitis occasionally occurring in chronic kidney disease may at times be difficult to differentiate."

Escat gives some plates to illustrate the pathological changes exhibited in an autopsy and urges the importance of everyone having the opportunity of making careful postmortem examinations in suspected cases. If Escat's reasoning be correct, we have a satisfactory explanation for many cases of deafness that have heretofore seemed very obscure. The prognosis and treatment is naturally that of general arteriosclerosis. Considering the symptoms separately, it may be said that deafness is the least curable, the tinnitus may become permanent, and the vertigo generally disappears. The best form of treatment Escat has found consists in the administration of hydrobromic acid in increasing doses while following the dietary of arteriosclerosis.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Experimental Anemias in the Rabbit.—C. H. BUNTING (*Jour. Exp. Med.*, 1906, viii, 625) has made an exceedingly careful study of the changes in the blood and bone-marrow of rabbits which have been subjected to injections of the hemolytic substances, ricin and saponin. The work was controlled by a study of the anemias produced by bleeding and by injections of substances acting differently from ricin and saponin. The results of these experiments are highly suggestive and aid to a

clearer understanding of the difference between a secondary and a primary anemia. Ricin has a marked toxic action on the blood elements, and when injected intravenously even in small doses in rabbits is quickly fatal. The destructive action on the leukocytes is evidenced by a rapid leukopenia, followed by a sharp reaction which reaches a considerable height at the end of twenty-four hours. During the stage of leukocytosis the white cells show signs of injury. With acute ricin poisoning the red cells are not greatly reduced in numbers, but in the circulation there appear enormous numbers of nucleated red blood corpuscles. The condition found in the bone-marrow serves to explain these changes. In the normal rabbit the cells of the bone-marrow are arranged in more or less definite groups which Bunting terms the erythrogenic and leukoblastic centres. The centres of the erythrogenic patches are composed of indifferent myeloblasts, while in the surrounding layers are megaloblasts, intermediate red cells, and normoblasts, and about the extreme periphery mature red blood cells. The white-cell centres are formed by layers of indifferent myeloblasts, myelocytes, and adult polymorphonuclear leukocytes. The marrows of the rabbits dying from ricin poisoning show marked depletion of many cells, and pycnosis and fragmentation of the remaining cells which go to form the proliferating centres for the red and white cells. This goes to show that ricin has a profound toxic action not only upon the cells of the circulation, but upon the cells of the bone-marrow. Here lies the essential difference between the secondary and primary anemias.

Rabbits bled on successive days developed a secondary anemia of moderate grade, with occasional nucleated red blood corpuscles in the circulation, but the marrow cells showed no injury. There was a proliferation of the erythrogenic centres in the normal manner.

Further experiments showed that by repeated injections of ricin a moderate grade of chronic anemia could be brought about in which the blood picture, except for a leukocytosis, resembled very closely that of pernicious anemia in man. Nucleated red blood corpuscles, usually normoblasts but often megaloblasts, were constantly present; macrocytes and microcytes formed a considerable percentage of the cells; and as the anemia progressed there appeared polychromatophilia and at times basophilia. By using saponin a chronic anemia could be produced which was even more strikingly like pernicious anemia, since there was a leukopenia with relative increase of the lymphocytes. In these cases the circulating blood often showed as many as 5000 to 10,000 nucleated red blood cells per cubic millimeter, 100 to 300 of which were megaloblasts. The lesions, confined almost exclusively to the bone-marrow in these cases of saponin poisoning, were of particular interest. Besides the injury to the cells there were large hemorrhages. Later, a great increase in connective tissue was found, which diminished greatly the space available for the hemopoietic tissue. So marked was this sclerosis that it was difficult to explain how the red count of 2,000,000 to 3,000,000 could be maintained. The explanation was found, however, in the fact that in the peripheral sinuses of the spleen there appeared to be a vicarious formation of red blood cells. The peripheral sinuses of the spleen were distended and crowded with cells, chiefly of the erythrogenetic series, though there were also megalokaryocytes and leukocytes. The nucleated red blood cells were

grouped much as they are in the marrow and showed numerous mitotic figures.

Bunting concludes that red-cell crises in the circulating blood are an expression of injury to the bone-marrow. When the mature erythrocytes about the periphery of the erythrogenic centres are depleted by hemorrhage, or the action of a circulating toxin, the bone-marrow reacts with nucleated cells. In the first case the reaction is much less marked than in the second. Following toxic injury to the marrow with destruction of the peripheral cells of the erythrogenic groups, there is established an atypical formation of erythrocytes resulting in pathological forms. When the marrow is extensively injured the spleen may take on the hemopoietic function. With subcutaneous injections of the hemolytic toxin the absorption is so slow that the toxin is apparently saturated by cells in the circulation and does not reach the marrow in sufficient quantity to injure it. Under those conditions there is blood destruction, but no nucleated red-cell crises in the circulation, and the marrow picture is one of hyperplasia, such as is seen after hemorrhage, that is, the marrow of a secondary anemia.

Studies upon Acromegaly, with Special Reference to the Connection between Acromegaly and Tumors of the Hypophysis.—Three hypotheses have been advanced to explain the connection between acromegaly and tumors of the hypophysis: (1) That the function of the hypophysis is partially or entirely destroyed; (2) that the function of the hypophysis is increased, and (3) that the acromegaly is primarily due to a disturbance of metabolism and that the hypophysis tumor is a symptom of the disease. CAGNETTO (*Virch. Arch.*, 1907, clxxxvii, 197) has already studied 2 cases of hypophysis tumor, in 1 of which, without acromegaly, the hypophysis was entirely destroyed by a sarcoma arising from another tissue; he now reports 3 more cases, describes enlarged hypophyses in 2 pregnant women. Acromegaly was present in the first 3 cases. A study of these cases and a review of the literature seem to throw much doubt upon the hypophysis theory of acromegaly, and especially upon the theory of "hypepitiutarismus" (hypersecretion of the hypophysis). Acromegaly occurs without hyperplasia of the glandular lobes of the organ; acromegaly may occur in association with a tumor free from functionating elements (chromophile cells); tumors of the hypophysis occur with numerous functionating cells in which there is no associated acromegaly.

Changes in the Bloodvessels and Organs brought about by Injections of Adrenalin Preparations.—The alterations in the walls of the arteries of rabbits, described first by Josué, in 1903, following injections of adrenalin, have now been produced by various observers and described in detail. They consist briefly of a necrosis in the middle coat followed by matting together of the elastic fibers that later on break up in fragments. Inflammatory reaction follows with infiltration by lymphocytes and the formation of giant cells. Subsequently there is calcification with thickening of the intima or aneurysmal bulgings. Recently v. KOVANJE (*Deut. med. Woch.*, 1906, No. 17) and BOVERI (*Deut. med. Woch.*, 1906, No. 22) have stated that the effects of the adrenalin injections may be greatly modified or partially neutralized by

simultaneous injections of iodine preparations. BILAND (*Deut. Arch. f. klin. Med.*, 1906, lxxxvii, 413) has repeated these experiments and comes to a different conclusion. Eighteen rabbits were injected subcutaneously with adrenalin hydrochloride. Of these, eight were also given doses of potassium iodide. One rabbit received thirteen injections of the iodide. The injections of the iodide did not seem to neutralize in the least the action of the adrenalin. Indeed, in the rabbits which received both potassium iodide and adrenalin it was found that the lesions of the bloodvessels were more marked than in the animals which received the adrenalin alone. Further studies were made to determine the effect which the adrenalin might have upon the blood pressure. The blood pressure of nine injected animals varied between 90 and 130 mm. Hg.; in the control animals the pressure varied between 85 and 110 mm. Hg. There was no parallelism between the height of the blood pressure and the extent of the vascular lesions. Immediately after the first injection of adrenalin the blood pressure rose to from 180 to 222 mm. Hg. Following this there was a rapid fall within five or seven minutes to normal. The effect of subsequent injections, even in very large doses, was much less marked, and a second injection, given before the blood pressure curve following the first had reached normal, produced no effect upon the regular descent. Though Biland could not determine that an increase of blood pressure played any part in the production of the vascular lesions, he could find evidence to show that the action of the adrenalin was dependent upon a toxic necrosis of the coats of the bloodvessels. In the kidneys more or less diffuse or localized areas of necrosis were encountered. They involved principally the epithelium of the tubuli contorti, and more rarely the loops of Henle. Occasionally there were calcium deposits, oftenest in the lumen of the tubuli contorti and tubuli recti. Not only are there evidences of an intoxication of the cells of the kidney, but toxins are eliminated in the urine. The urine from rabbits treated with adrenalin was highly toxic, and in doses of 0.5 to 1 cm. it was fatal to healthy animals, which died in tetanic convulsions. The injections of toxic urine caused a marked decrease in blood pressure, and in other ways acted quite differently from adrenalin, so that Biland concludes that its injurious effect is not due to the elimination of adrenalin by the kidneys.

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THE

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OF THE

MEDICAL SCIENCES.

EDITED BY

A. O. J. KELLY, M.D.

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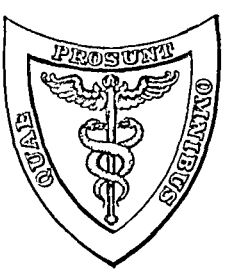

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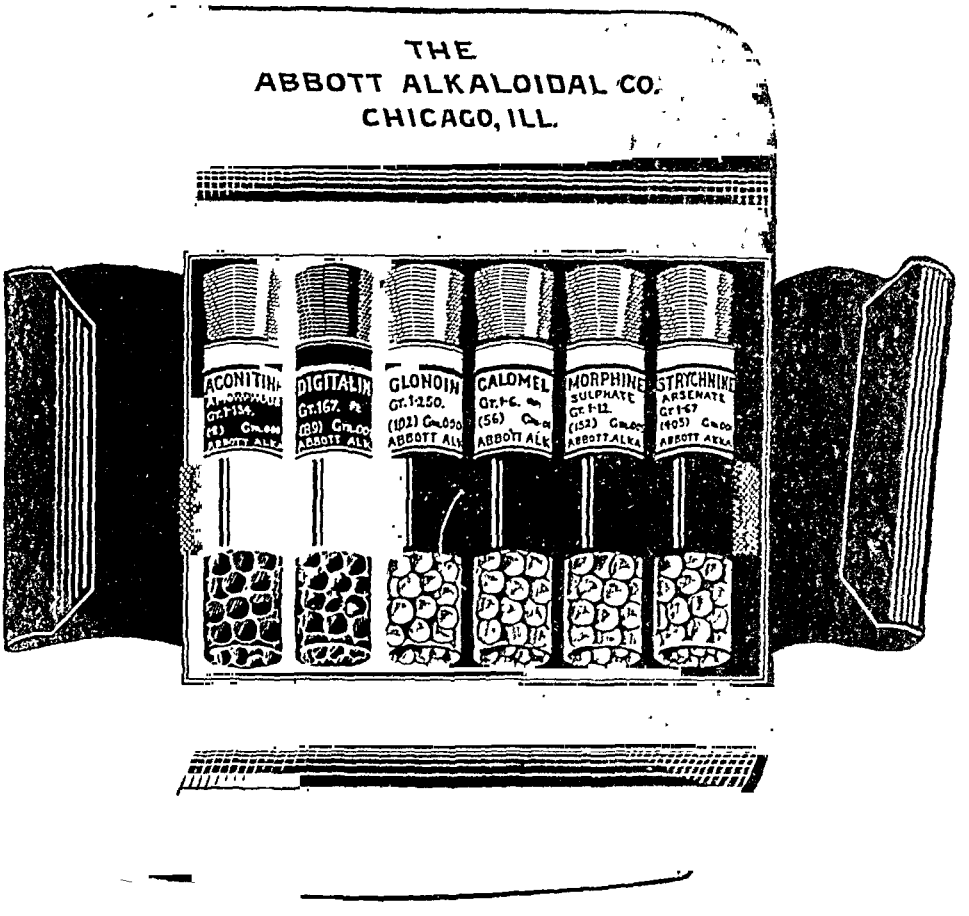

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